THE CANCER LETTER

Vol. 31 No. 46
Dec. 16, 2005

Price $335 Per Year

Ethicists Dispute Von Eschenbach's Claim That His NCI-FDA Conflicts Are Managed

By Paul Goldberg

Addressing the National Cancer Advisory Board last week, Andrew von Eschenbach said his duties at NCI and FDA aren't in conflict, because he has no direct responsibility for development of cancer therapies at the institute.

"Here at the NCI, the issues and the decisions having to do with agents, devices, drugs that we may… hold the [Investigational New Drug licenses] for… are done at a level of the institution that I don't directly influence or control," von Eschenbach said at the NCAB meeting Dec. 6.

NCI holds the INDs for many cancer therapies, likely more than any drug company. According to critics, this means that FDA Acting Commissioner von Eschenbach is responsible for regulation of NCI Director von Eschenbach.

(Continued to page 2)

In Brief:

Former Bristol-Myers Executive Bruce Ross To Replace William Rastetter At Biogen Idec

BRUCE ROSS was named nonexecutive chairman of **Biogen Idec Inc.** of Cambridge, Mass., replacing executive chairman **William Rastetter**, who will retire Jan. 1. Ross, a former Bristol-Myers Squibb executive who directed oncology, and founding CEO of the National Comprehensive Cancer Network, has been on the IDEC board since 1997. IDEC and Biogen merged in 2003, and the company's biggest product is Rituxan (rituximab), which generated $1.6 billion in U.S. sales last year. "I am proud to have been at Bristol-Myers when that company was the leader in developing cancer therapies and I'm equally proud to be affiliated with Biogen Idec at a time when our company and the entire biotechnology industry is making significant contributions to treatments for serious diseases such as cancer, multiple sclerosis, and rheumatoid arthritis," Ross said. **James Mullen** will continue as president and CEO of Biogen Idec. . . . **LUSTGARTEN FOUNDATION for Pancreatic Research** announced two appointments. **Robert Mayer** was named chairman of the scientific advisory board and **Ralph Hruban** was named science director, the first for the foundation. Mayer, director of the Center for Gastrointestinal Oncology at Dana-Farber Cancer Institute and a physician at Brigham and Women's Hospital and Massachusetts General Hospital, will oversee the medical and research efforts for the foundation. He also is chairman of the Gastrointestinal Cancer Committee of the Cancer and Leukemia Group B. Mayer succeeds **Joseph Simone**. Hruban is professor of pathology and oncology and director of the

(Continued to page 7)

Publication Break:
The Cancer Letter will take its annual winter publication break for the next three weeks. The next issue is scheduled for publication Jan. 13. The Cancer Letter is published 46 times a year.

NCI-FDA Head Appears To Cite Klausner-Era "In-Box Rule"

(Continued from page 1)

Von Eschebach's statement to NCAB appears to be an adaptation of a controversial legal interpretation formulated by HHS attorneys in 1997 to pave the way for then-NCI Director Richard Klausner to accept the Dickson Prize in Medicine and a check for $40,000 from the University of Pittsburgh.

At the time, a top HHS ethics official opined that ethics rules didn't preclude Klausner from accepting a monetary award from an NCI-funded institution, because routine matters of Pitt's interaction with the institute didn't reach Klausner's desk.

The interpretation—called the "in-box rule," because it relied on the official's in-box to gauge potential conflicts—figured prominently in the May 18, 2004, hearings of the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce.

At the hearing, the top HHS ethics official portrayed the in-box rule as a symptom of lax ethics in the Clinton administration. "I can assure you that we don't operate under this type of advice under the current administration," said Edgar Swindell, the HHS Assistant General Counsel for Ethics. Swindell is also the official who signs off on von Eschenbach's ethics documents.

Von Eschenbach's assertion that he wouldn't encounter conflicts of interest at FDA, because he doesn't directly influence or control NCI's handling of the INDs, differs from his previous statement on management of conflicts of interest.

In a Sept. 30 memorandum to FDA employees, von Eschenbach wrote that "as a prudential matter" he would refrain from participation in "certain FDA matters in which NCI is a party, unless the Department requests that I participate on a case-by-case basis."

In that memo, von Eschenbach pledged to take no part in:

—"Approval applications affecting drugs, devices, and biologics submitted by NCI or where an NCI employee was a principal investigator;

—"FDA oversight/observation of adverse event reporting in NCI clinical protocols;

—"Other matters involving NCI as a party in which FDA is exercising its regulatory authority."

The caveat "unless the Department requests that I participate on a case-by-case basis" constitutes a loophole that makes the memo into a "Recusal Lite," an ethics expert said at the time (The Cancer Letter, Oct. 7). Now, the loophole may have grown wider. If von Eschenbach is indeed guided by the reasoning of the in-box rule, he could take part in any matter that doesn't end up in his direct purview—his in-box—at either NCI or FDA.

Statements Deepen Ethics Concerns

"There is certainly a potential for conflicts of interest here—seemingly a large potential," said Margaret McLean, director of the biotechnology and healthcare ethics program at the Markkula Center for Applied Ethics and senior lecturer in religious studies at Santa Clara University. "We all deal with conflicts of interest all the time—the key question is whether or not these conflicts can be managed. This seems to be questionable in this case.

"Von Eschenbach seems to find himself in situations that raise concerns about fairness in decision-making," McLean said. "It seems to me that being part of the Public Health Service places special obligations on the NCI and the FDA to be concerned first and foremost with the public's health. It would seem that, however best intentioned, conflicts here would be inevitable, and at some point, unmanageable. And, of course, the perception of conflict, which seems unavoidable here, can be more damaging than actual conflict, since the perceptions cannot be effectively managed."

Von Eschenbach's invocation of the in-box rule is unconvincing, said Paul Light, a scholar of governance

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

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.

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
Customer service FAQ: www.cancerletter.com

Subscription $335 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

studies at Brookings Institution and Paulette Goddard Professor of Public Service at New York University.

"A reasonable reading is that every decision he makes will affect himself, either directly or indirectly," said Light, who is also a senior adviser to the Brookings Presidential Appointee Initiative. "The conflict comes from the conscious or subconscious influence that his association with NCI creates. Being FDA commissioner is no small job—its responsibilities are great, and its reach even greater. To assume that NCI will somehow not be affected by the commissioner's decisions, and vice versa, is nonsense."

The conflicts between von Eschenbach's positions are likely to translate into risks to which participants in clinical trials would be exposed, ethics experts say.

"The guiding principle here should be 'do no harm,' which includes not putting patients in harm's way," McLean said. "It may be that unavoidable conflicts in this case would put patients at risk. In that case, wearing these two hats is quite problematic."

Since NCI holds INDs for cancer therapies, von Eschenbach's dual role could undermine public trust in clinical trials, Light said.

"I can't imagine that any patient who learns that the FDA commissioner still has ties to a major investigational drug firm could feel anything but unsettled," he said. "This is no place for even the slightest hint of conflict of interest, whether real or implied. Isn't the rule 'first do no harm?'

"The Senate and White House should think of the millions of patients who might second-guess their therapies as a result of the new commissioner's dual role."

Not A Proud Chapter In Government Ethics

Government ethics laws define conflicts of interest in terms of personal, usually financial, interests on the part of an official.

Von Eschenbach's conflicts are different. They stem from his dual employment, and since no one has ever run NCI and FDA before, full implications of these conflicts are unexplored.

Von Eschenbach said recently that a team of six lawyers is monitoring his actions (The Cancer Letter, Nov. 23).

However, it's unclear whether any formal recusal documents have been drafted to guide von Eschenbach on ethics. HHS ethics officials declined to talk with this reporter, and department spokesman Christina Pearson didn't respond to e-mailed questions that sought to establish whether such papers exist.

Invoking the principles of the in-box rule would be a puzzling choice for von Eschenbach, considering that at an Oversight & Investigations hearing last year, HHS attorney Swindell delivered a mea culpa about using the in-box rule in Klausner's situation.

"I am the one that signed that approval, and it is not a decision that I look back on with fondness and pride," Swindell said at the hearing.

At the time Klausner received the Dickson prize, HHS lawyers were instructed to refrain from considering any appearances of conflicts of interest, paying attention only to actual conflicts, Swindell testified. Negative determinations could be given only in cases where no other answer was possible, he said.

Swindell said that in 1997, he was pressured by then HHS General Counsel Harriet Rabb to allow Klausner to accept the money. "I don't know why this was so special, but it was, obviously," Swindell said at the hearing last year. "She was somewhat inscrutable, because she also seemed to understand that this was unseemly… She would frown about the fact [that] he is trying to make a big deal about getting some money."

Bowing to pressure, Swindell crafted an opinion that created the in-box rule. In the Oct. 7, 1997, memo to Klausner, the ethics attorney wrote that the "scope of the emplyee's official duties" is a criterion for judging conflicts. "Does the position description normally encompass handling the types of matters that are pending?" he wrote. "For example, is the final sign-off on a pending grant delegated to another agency official?"

After Swindell issued this opinion, Klausner and other NCI employees were able to justify receiving awards from grantee institutions. Recently, Klausner said the in-box rule also covered his job negotiations with Harvard University at a time when NCI was considering a proposal to fund a $40 million contract with a lab at that institution.

"That was how I recall the advice we were given," Klausner wrote in an e-mail to The Cancer Letter. "It was called the 'in-box rule' and related to action items 'in your in-box'" (The Cancer Letter, Sept. 16). The committee and the Government Accountability Office are continuing their investigation of Klausner (The Cancer Letter, Sept. 9).

The in-box rule clearly failed to withstand scrutiny of the House committee that oversees both NCI and FDA.

"I believe it would strain credibility to argue that a grantee regularly receiving millions of dollars in grants from a federal agency is 'detached from' or

'disinterested in' or 'independent of' the duties, powers, and responsibilities of the director of that agency," testified Jack Maskell, a legislative attorney with the American Law Division at the Library of Congress Congressional Research Service,

"Even when the agency head or other supervisory personnel are not directly participating in the award of a grant, or actually participating in certifying the private entity as a 'comprehensive' treatment facility, the actual authority over those subordinate employees making the decisions, promotion, pay and work assignments and other things.

"The inherent influence of supervisors and agency heads over such subordinate employees, and the natural inclination of employees to want to please their supervisors, all counsel against such agency heads and management personnel receiving cash awards from these private grantees under the regulation," Maskell said. "In fact, if there is a particular matter pending before the official relating to the private entity at the time of the cash payments, questions of both application of criminal law as well as ethics violations could be implicated."

Also testifying at the hearing, Marilyn Glynn, then acting director of the Office of Government Ethics, said her office hasn't issued any blanket guidance documents on the acceptance of awards from grantee institutions.

"The approach we would follow… is one of reasonableness," Glynn testified. "Is it reasonable to assume that the office head may become involved in a matter substantially affecting the interests of the donor, or is the chance of such intervention simply a remote and speculative possibility?"

Glynn described the criteria for making such determinations:

—"How have such matters been handled historically by the office? For example, is there precedent for the office head becoming involved in matters of this type and/or matters involving this particular donor in the past? Are matters of this type typically handled at a level far below the office head, or are they handled at an intermediate level somewhat closer to the agency head?

—"How large is the office for which the employee is responsible?

—"Is there a multitude of similar matters pending somewhere in the office at any given time, such that the matter affecting the donor may be less likely to have any particular prominence?

—"How important or sensitive is the matter? For example, does the matter involve a significant dollar amount or is there any particular controversy or novelty? On the other hand, is the matter relatively routine and one that does not call for the exercise of significant discretion?

—"Is the office head typically apprised of such pending matters and any attendant issues, for example, through status reports that identify the affected source?

—"Can it be said that the donor is a regular 'constituent' or 'stakeholder' with respect to the programs and operations of the office? For example, does the particular donor have a number of matters pending in the office or does the donor regularly seek business or official action from the office?"

The hearing transcript is available at http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=108_house_hearings&docid=f:93973.wais.

Conflicts Extend To Regulated Industry

Following criticism of his dual appointment nearly three months ago, von Eschenbach said he would take a leave of absence at NCI and concentrate on his duties at FDA. However, he has continued to show up at his NCI office, take part in the institute's meetings with advisors and outside groups, and travel in his capacity as NCI director.

At FDA, von Eschenbach said he would "streamline and accelerate" the process of approval of therapies, and announced that the regulatory agency has joined NCI in pursuit of his controversial goal to "eliminate the suffering and death due to cancer by 2015" (The Cancer Letter, Oct. 21). Neither of these goals appears to be consistent with even a limited recusal from matters that involve NCI, observers say.

Von Eschenbach's association with non-profits heavily funded by the pharmaceutical industry created additional problems for the NCI director and FDA acting commissioner.

Through his four years at NCI, von Eschenbach served as a fiduciary of C-Change, an industry-funded coalition. To enable him to serve on that board in his official capacity as NCI director, HHS waived conflict of interest statutes.

Experts in government ethics who were asked by The Cancer Letter to review the waiver granted to the NCI director said that the document failed to provide a compelling justification for allowing him to serve on the board. The waiver, signed by Swindell, is posted at http://www.cancerletter.com/archives/post.html?http://www.newslettersonline.com/user/user.fas/s=292/fp=3/tp=18?T=open_article,901522&P=article.

Experts in ethics said von Eschenbach was facing a three-way conflict between his roles at NCI, FDA, and C-Change (The Cancer Letter, Sept. 30).

Von Eschenbach resigned from the C-Change post after a story about these conflicts was published in The Cancer Letter and was widely quoted in the press (The Cancer Letter, Oct. 7).

Von Eschenbach is also an endorser and a member of the CEO Roundtable on Cancer, another coalition funded by pharmaceutical companies and run by their top executives (The Cancer Letter, Nov. 23).

Three weeks after von Eschenbach's role with the CEO Roundtable was reported by this publication, his photo and his endorsement remain on that group's web site: www.cancergoldstandard.org.

NIH Programs:

The Cancer Genome Atlas Is New Name For NCI-NHGRI $100M Sequencing Project

By Kirsten Boyd Goldberg

NIH earlier this week announced a $100-million project to sequence cancer genomic changes, unveiling the project's new name: The Cancer Genome Atlas.

Though grant applications for the new project aren't being accepted yet and the tumor types to be studied haven't been selected, NIH brought out top officials for a press conference Dec. 13 in Washington to give the effort a public "launch."

The press conference took place as Congress was reconciling the House and Senate versions of the fiscal 2006 appropriations bills. Biomedical organizations urged Congress to approve the Senate version of the Labor-HHS appropriations, which would provide NIH $29.4 billion, a 3.7% increase from last year.

NIH officials said funding for the new program is included in the budgets of NCI and the National Human Genome Research Institute, which are providing $50 million each for the pilot project. Last month, the NCI Board of Scientific Advisors voted to approve the program, previously known as the Human Cancer Genome Project (The Cancer Letter, Nov. 18).

The long-term goal is to characterize most of the genetic mutations responsible for many types of common cancers, but the effort would begin with a three-year pilot project to determine the feasibility of large-scale gene sequencing.

"This is an audacious undertaking," NHGRI Director Francis Collins said. "You remember when people were skeptical that we could determine the genome of just one individual. We're talking about basically thousands of Human Genome Projects."

However, "the time is right to bring the full power of genomics to bear on the problem of cancer," Collins said. The program's new acronym, TCGA, represents the first letters of human DNA. That's "kind of appealing," said Collins. Also, "the concept of an atlas… does pull up in people's minds the kind of image, the kind of metaphor, that we hope to convey of what this project is all about," he said.

"This is something that absolutely needs to be done now," NIH Director Elias Zerhouni said. The project will be successful if it provides "proof of concept that intelligently designed, multi-targeted approaches do work in cancer," he said. "That, I think, would be a breakthrough. It won't take 15 years. It's a recombination of things we have in hand, which we do not know how to use optimally."

NCI Director and Acting FDA Commissioner Andrew von Eschenbach said the project is about "the progress that is necessary in order for us to make cancer a manageable chronic condition."

The project would eventually help scientists develop "a new generation of diagnostics and therapeutics for cancer," said Anna Barker, NCI deputy director for advanced technologies and strategic partnerships. Barker said genomic analysis "on a smaller scale, is already impacting patients" through the ability to segment types of cancer and predict outcomes of therapy. "This will speed it up," she said.

Under the project, a Human Cancer Biospecimen Core Resource will collect and process cancerous and healthy, control tissue samples.

NCI has asked biospecimen repositories for information on whether existing collections can be used retrospectively to provide the specimens needed for the TCGA. The project has "very strict criteria" for homogeneous tumors collected as part of clinical trials, Barker said.

"The goal is to choose tumors that will optimize our chance of success," Barker said. The tumors should have "as little contamination from normal cells as possible," and the tumor samples must be relatively large, she said.

The samples will be distributed to Cancer Genome Characterization Centers and Genome Sequencing Centers that will be established for identification of genomic targets and high-throughput sequencing. These centers would be selected in 2006.

The first-year budget for the Cancer Genome Characterization Centers has been set at $11 million,

with an additional $2 million for the development of new technologies. About $16.7 million will be devoted to the TCGA at the Genome Sequencing Centers during the pilot's first year.

The data from the centers will be deposited in public databases. If the pilot project is successful, the data would provide the beginning of an "atlas" describing the genomes of all cancers. A subcommittee of the National Cancer Advisory Board estimated the project could cost $1.35 billion over 10 years.

Collins said it is too early to estimate the full cost of the project. "If it is as successful as many of us believe it will be… we will then contemplate what could be done to scale it up to look not just at two or three tumor types, but maybe as many as 50," he said. "The exact cost of that will be impossible to predict right now, because we don't know what the course of development of the technologies that we're going to try during the pilot phase will be.

"We obviously count upon the fact that having a pilot of this sort is a strong inspiration for the development of new technologies and the optimization of existing ones, just as was the case for the genome project," Collins said.

Critics have warned that the large-scale project could use funds better spent on individual investigator-initiated grants. Zerhouni said NIH would maintain its number of grants. "As far as priorities at NIH, I've stated publicly and I state again that the number one priority is to maintain the ability of fresh ideas and new investigators to come into the field of life sciences," he said.

Larger projects such as TCGA "provide new opportunities for new hypotheses that these researchers will use," Zerhouni said. "So as a matter of policy, the tough choices we will make in terms of large projects and their costs are going to be made in full recognition of the potentially deleterious impact it can have on individual investigators."

Further information about the TCGA is to be posted at http://cancergenome.nih.gov.

Professional Societies:

AACR Workshop Advocates Human Epigenome Project

By Kirsten Boyd Goldberg

In the same week that NIH announced The Cancer Genome Atlas, a group of cancer scientists issued a call for another large research project, an international Human Epigenome Project designed to map the chemical modifications to DNA that comprise the epigenetic code.

The epigenome consists of chemical "amendments" that dangle from the linear string of letters that spell out the genetic code. Epigenetic aberrations can play a role in aging, mental health, and cancer, said a group of 40 scientists who proposed the project.

The proposal, "A Blueprint for a Human Epigenome Project," was published in the Dec. 15 issue of Cancer Research. It summarized a workshop held last June by the American Association for Cancer Research.

"Definition of the human epigenome and its application to developing diagnostic, prognostic, and therapeutic tools will likely produce some of the earliest translational research benefits flowing from large-scale genome initiatives to the bedside," said Frank Rauscher III, editor-in-chief of Cancer Research. "It is time to create a concerted international effort to unlock the epigenomic information stored in our genome and use it for the benefit of human health."

Technologies are available that make the project feasible, the report's authors said.

"One of the most exciting points to emerge from the meeting is that the technology needed for doing epigenetics on a high-throughput basis has advanced so far that people are already engaged in epigenomic studies on a piecemeal basis," said AACR President Peter Jones, director of the Norris Comprehensive Cancer Center at the University of Southern California. "A coordinated, large-scale Human Epigenomic Project would pave the way for unforeseen breakthroughs in understanding normal and disease states."

Epigenetic profiles differ among tissues, individuals, and healthy vs. disease states. The workshop participants advocated choosing a small number of "reference" epigenomes to be analyzed at a high level of resolution. Tissues proposed for this analysis include peripheral blood cells and foreskin fibroblasts.

A much larger group of samples could be examined using a lower-resolution "scanning" approach that would help delineate basic principles of epigenetic effects on gene activity, the participants said. The scanning approach would point out areas that should be "drilled down" with additional study.

The goal of the project would be "to identify all the chemical changes and relationships… that provide function to the DNA code, which will allow a fuller understanding of normal development, aging, abnormal gene control in cancer and other diseases, as well as the role of the environment in human health," the report said.

In Brief:

Penn Receives $25 Million Pledge For Medical Center

(Continued from page 1)

Division of Gastrointestinal/Liver Pathology at The Johns Hopkins University School of Medicine and founded the National Familial Pancreas Tumor Registry. . . . **PENN Medicine Center for Advanced Medicine** at the University of Pennsylvania received a $25 million pledge from alumnus Raymond Perelman and his wife, Ruth, to rename the center The Raymond and Ruth Perelman Center for Advanced Medicine. Perelman, a PENN Medicine trustee, is president and chairman of the board of RGP Holdings Inc. The clinical space will house the Penn Abramson Cancer Center, radiation oncology, cardiovascular medicine, and an outpatient surgical pavilion. The gift will finance the construction and completion of the center. . . . **DANA-FARBER CANCER INSTITUTE** received $16.5 million from John and Shelley Blais for the Blais Proteomics Center to study cellular protein for diagnosing, treating and preventing cancer. The gift brings to more than $30 million the amount that the Blais family has contributed to Dana-Farber to support protein research and other initiatives. The donation allows the purchase of mass spectrometers, funding of a program to design new experimental methods and improve mass spectrometry technology, and support for the design of mathematical models for high-volume data analysis. Blais, a trustee at Dana-Farber, is the founder and president of BlaisCo LLC of Framingham, a holding company specializing in high-technology firms. . . . **CITY OF HOPE CANCER CENTER** received a four-year $14 million NCI Survivorship Grant to train 400 cancer caregivers in surveillance and follow-up care. The three-day annual seminars will be hosted near City of Hope from 2006 through 2009. **Marcia Grant**, research scientist and director of the Department of Nursing Research and Education, is principal investigator for the project, known as Survivorship Education for Quality Cancer Care. Participants' training will be based on a conceptual model featuring four dimensions of cancer survivorship: physical well-being and symptoms; psychological well-being; social well-being; and spiritual well-being, said Grant. The model was created by Grant and her colleagues, **Betty Ferrell**, co-investigator, and **Smita Bhatia**, staff physician and director of epidemiology and outcomes research, Division of Pediatrics. . . . **DAN MERCOLA**, professor of pathology and laboratory medicine in the School of Medicine at the University of California at Irvine, received a five-year, $9.5 million grant from NCI to develop a genetic method for predicting the outcome of prostate cancer at the time of diagnosis. Mercola will lead a multi-institute collaboration, which will include researchers from UC San Diego, the Sidney Kimmel Cancer Center in San Diego, the Burnham Institute for Medical Research and the Scripps Research Institute, Northwestern University, the Translational Genomics Research Institute, and Sun City Health Institute. . . . **COLUMBUS CHILDREN'S HOSPITAL**, **Cincinnati Children's Hospital Medical Center,** and **Ohio State University Comprehensive Cancer Center** have signed a collaborative agreement to establish the Pediatric Oncology Program to broaden the study of childhood cancer and accelerate the transfer of research findings to the clinical setting. Specific objectives include the development of a joint strategic plan for cancer research and education and to utilize more fully the resources of each institution and its researchers in the region. **Michael Caligiuri**, director of Ohio State University's Comprehensive Cancer Center, will serve as director of the effort, along with co-directors from Cincinnati Children's and Columbus Children's. The Pediatric Oncology Program is being established as part of the National Cancer Institute-designated Comprehensive Cancer Center at OSU. "The partnership combines the unique and complementary strengths of three well-known and powerful cancer research institutions in Ohio to address pediatric cancer," said **Linda Weiss**, chief of the NCI Cancer Centers Branch. . . . **UMDNJ-Robert Wood Johnson Medical School** researchers received grants totaling $670,000 from The Breast Cancer Research Foundation. **Arnold Levine**, professor of pediatrics and biochemistry, UMDNJ-Robert Wood Johnson Medical School and resident member, Cancer Institute of New Jersey, and **Sandra Harris**, instructor, Department of Pediatrics, UMDNJ-Robert Wood Johnson Medical School and CINJ researcher, received $500,000 for their work on gene mutations and cancer. **Antoinette Tan**, assistant professor of medicine, UMDNJ-Robert Wood Johnson Medical School and CINJ medical oncologist, received $170,000 for her research on newly diagnosed breast cancer. BCRF was established in 1993 by Evelyn Lauder, senior vice-president, The Lauder Companies Inc. . . . **FOX CHASE CANCER CENTER** announced staff appointments. **Barbara Burtness** joined the Division of Medical Science. She was associate professor in internal medicine and director of the gastrointestinal oncology unit at Yale University. **Lionel Lima** was named associate vice president of cancer services for

The Henry Cancer Center at Geisinger Wyoming Valley. The cancer program at HCC is a partnership between Geisinger Health System and Fox Chase Cancer Center. Lima was director of clinical and administrative services at Temple University Hospital, where he developed the oncology service line.

Funding Opportunities:

Leukemia Foundation New Investigator Grants

$100,000 One-Year Leukemia Research Foundation New Investigator Scientific Grants

Deadline for Submission: Dec. 10.

Leukemia Research Foundation invites applications for its one-year New Investigator Scientific Grants, which have been increased to $100,000, effective immediately. Applicants must be U.S. citizens. Research projects undertaken outside the U.S. will be considered. The funding cycle will begin July 1. Guidelines, application and information is available at Grants@LRFMail.org. or www.leukemia-research.org/phd.

RFAs Available

RFA-CA-06-004: Innovations in Cancer Sample Preparation

Letters of Intent Receipt Date: March 11.

Application Receipt Dates: April 11.

NCI invites applications for research in the development and significant enhancement or adaptation of sample preparation methodologies and technologies, the development of assays to assess sample quality, and studies designed to elucidate the criteria by which to judge sample quality. The outcome will be products and methods designed to optimize sample utility. Samples may originate from residual material not necessary for patient care or from cell lines, model organisms, or other sources relevant to cancer research.

Support will be through the NIH Exploratory/ Developmental Research Grant R21, the Exploratory/ Developmental Research Grant Phase 2 R33, and the Phased Innovation Award R21/R33 mechanisms. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-003.html.

Inquiries: Inquiries: Gregory Downing, 301-496-1550; downingg@mail.nih.gov.

RFA-CA-07-005: Advanced Proteomic Platforms and Computational Sciences for the NCI Clinical Proteomic Technologies Initiative

NCI invites applications for proteomic technology research to be applied for the measurement of proteins and peptides in clinical cancer studies. The funding opportunity, which will be the R21 Exploratory/Developmental Award or the R21/R33 Phased Innovation Award, will focus on two areas. The first area is technology for protein and peptide detection, recognition, measurement, and characterization in biological fluids that will overcome current barriers in protein/peptide feature detection, identification, quantification, and validation. The second focus area supports computational, statistical, and mathematical approaches for the analysis, processing, and facile exchange of large proteomic data sets. Support will be through the NIH Exploratory/Developmental Research Grant R21, the Exploratory/Developmental Research Grant Phase 2 R33, and the Phased Innovation Award R21/R33 mechanisms The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-005.html.

RFA-CA-07-001: Innovative Technologies for Molecular Analysis of Cancer

Letters of Intent Receipt Date: Jan. 23; April 26

Application Receipt Date: Feb. 22; May 26

NCI invites applications for research projects encompassing methods and tools that enable research, including, but not limited to, instrumentation, techniques, and devices. Technologies solicited include those that are suitable for the detection of alterations and instabilities of genomic DNA; measurement of the expression of genes and gene products, including proteins; analysis and detection of gene and/or cellular products, including post-translational modification and function of proteins; identification and characterization of exogenous infectious agents in cancer; and assaying the function of major signal transduction networks involved in cancer. Developing technologies would include those that will support molecular analysis in vitro, in situ, or in vivo in discovery processes as well as in pre-clinical models and clinical research. Funding will be through the NIH Exploratory/Developmental Research Grant R21, the Exploratory/Developmental Research Grant Phase II R33. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-001.html.

Inquiries: Gregory Downing, 301-496-1550; downingg@mail.nih.gov.

RFA-CA-07-002: Application of Emerging Technologies for Cancer Research

NCI invites applications to evaluate the usefulness of emerging molecular technologies that are ready for initial application to clinical or biological questions in cancer research. Projects should demonstrate that the technology is robust and yields reproducible measurements. Projects should also be designed to gather preliminary data to support the use of the technology in a future project with a clinical or biological focus. In addition, applications that propose the use of commercially available technology under standard conditions, or any technology that is already commonly accepted for the proposed use, are not appropriate. The funding opportunity will use NIH R21 Exploratory/ Developmental award, R21/R33 Phased Innovation award, and the R33 Exploratory/Developmental Phase II award mechanisms. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-002.html.

Copying Policy for The Cancer Letter Interactive

The software that comes with your issue allows you to make a printout, intended for your own personal use. Because we cannot control what you do with the printout, we would like to remind you that routine cover-to-cover photocopying of The Cancer Letter Interactive is theft of intellectual property and is a crime under U.S. and international law.

Here are guidelines we advise our subscribers to follow regarding photocopying or distribution of the copyrighted material in The Cancer Letter Inc. publications in compliance with the U.S. Copyright Act:

What you can do:

--Route the printout of the newsletter to anyone in your office.

--Copy, on an occasional basis, a single story or article and send it to colleagues.

--Consider purchasing multiple subscriptions. Contact us for information on multiple subscription discounts.

What you can't do without prior permission:

--Make copies of an entire issue of the newsletter. The law forbids cover-to-cover photocopying.

--Routinely copy and distribute portions of the newsletter.

--Republish or repackage the contents of the newsletter.

We can provide reprints for nominal fees. If you have any questions or comments regarding photocopying, please contact Publisher Kirsten Boyd Goldberg, phone: 202-362-1809.

We welcome the opportunity to speak to you regarding your information needs.

THE CANCER LETTER

Vol. 20 No. 11
December 2005

Business & Regulatory Report

Deals & Collaborations:

Amgen To Buy Abgenix For $2.2 Billion; Deal Gives Amgen Panitumumab

Amgen (Nasdaq: AMGN) of Thousand Oaks, Calif., and **Abgenix Inc**. (Nasdaq: ABGX) of Fremont, Calif., signed a definitive merger agreement under which Amgen will acquire Abgenix for $2.2 billion in cash plus the assumption of debt.

Under the agreement, shareholders of Abgenix will receive $22.50 in cash per share, about a 54% premium over stock trading price, the companies said.

The acquisition of Abgenix provides Amgen with full ownership of

(Continued to page 2)

Clinical Trials:

Cell Therapeutics To Begin Trial Of Xyotax Versus Paclitaxel For Advanced NSCLC

Cell Therapeutics Inc. (Nasdaq and MTAX: CTIC) of Seattle said it would begin a clinical trial of Xyotax, paclitaxel poliglumex, versus paclitaxel chemotherapy PS2 for chemotherapy-naive advanced stage non-small cell lung cancer.

The trial, known as PIONEER 1, is the first approval trial for lung cancer for women and would enroll 600 patients over the next 12 to 14 months, the company said.

"Gaining a better understanding of the biological role of estrogen in the development and progression of lung cancer has become increasingly important, especially with the growing number of women, including non-smokers, being diagnosed often at younger age than men and with different outcomes than men," said Kathy Albain, professor of medicine, hematology/oncology and director, thoracic oncology and breast clinical research, Loyola University Health System, and chairman of the PIONEER 1 trial steering committee. "Outcomes would be instrumental in developing tailored therapies, possibly based on gender but even more so, on the molecular biology of the disease. The exploratory data from the initial Xyotax studies are provocative and validate the design of the PIONEER 1 prospective study."

The exposure of lung cancer cells to estrogen increases the gene expression of cathepsin B, a critical enzyme that metabolizes Xyotax, releasing active paclitaxel within the tumor cell," said Suresh Ramalingam, assistant professor of medicine, University of Pittsburgh Cancer Institute. "The data suggest that normal estrogen levels may be beneficial due to the

(Continued to page 4)

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

Amgen Deal Also Cancels Royalty Payment To Abgenix

(Continued from page 1)

panitumumab, an IgG2 monoclonal antibody, which binds with high affinity to the EGFr. Panitumumab is in trials as a monotherapy and in combination for colorectal, lung, and kidney cancers.

Working with Abgenix under a development agreement that Amgen assumed as a result of its acquisition of Immunex Corp. in 2002, Amgen has led the development and commercialization strategy for panitumumab, the company said.

Also, the acquisition eliminates a tiered royalty that Amgen would have paid to Abgenix on future sales of denosumab (formerly AMG 162), an agent currently being studied for a broad range of bone loss conditions, including osteoporosis, treatment induced bone loss, bone metastases, multiple myeloma, and rheumatoid arthritis, the company said.

"Abgenix is a natural strategic fit for Amgen, given our strong existing relationship," Kevin Sharer, Amgen president and CEO, said in a statement. "Amgen has been intimately involved in all aspects of the development and commercialization of panitumumab over the last few years, providing us with substantial and realistic insight into the value of, and significant opportunities for, this cancer therapeutic. This investment reflects Amgen's commitment to our pipeline and our growing confidence in the future success of both panitumumab and denosumab."

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

World Wide Web: http://www.cancerletter.com

Business & Regulatory Report
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
PO Box 40724, Nashville TN 37204-0724

Business & Regulatory Report is a supplement to The Cancer Letter and available separately for $175 per year. ISSN 1053-9611.

Amgen and Abgenix said they plan to initiate a Biologics License Application with FDA for panitumumab in metastatic colorectal cancer patients who have failed standard chemotherapy.

"We believe this transaction will allow us to advance panitumumab to its full potential for patients and to maximize the value of both Abgenix's growing portfolio of antibody product candidates and our exceptional scientific platform," said Bill Ringo, Abgenix president and CEO.

The transaction includes the Abgenix 100,000 square foot manufacturing plant in Fremont, Calif., which will produce panitumumab and add to Amgen's protein manufacturing capabilities. Abgenix assets also include the proprietary fully human monoclonal antibody technology, XenoMouse.

* * *

American Pharmaceutical Partners Inc. (Nasdaq: APPX) of Schaumburg, Ill., and **American BioScience Inc.** of Santa Monica said they have signed a definitive merger agreement to merge ABI into APP to create a fully integrated, global biopharmaceutical company.

The all-stock transaction, which would combine the two companies under a new name, Abraxis BioScience, is expected to close in the first half of next year. ABI said it owns 64.4 percent of the outstanding fully diluted shares of APP.

APP's assets include the oncology drug Abraxane, a product pipeline and a hospital-based injectables business with positive operating cash flow, the companies said. ABI said it would bring to the new company 50 percent of the profits from North American sales of Abraxane as well as the marketing rights worldwide. A regulatory filing for the drug has been submitted in Canada. Regulatory filings in Europe and Mexico are expected next year and other countries, including China, Russia, Korea, Australia, New Zealand, Hong Kong and Taiwan, in 2006 and early 2007, the companies said.

Under the agreement, ABI would merge into APP in a tax-free transaction, the company said. In the merger, APP would issue to the ABI shareholders 86 million additional shares of APP common stock raising the ABI shareholders' fully diluted ownership of the combined entity after the merger to approximately 83.5 percent from 64.4 percent owned through ABI, the companies said.

FDA approved Abraxane in January for breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of anthracycline-containing adjuvant chemotherapy.

* * *

BioWa Inc. of Princeton, N.J., said **MedImmune Inc.** (Nasdaq: MEDI) of Gaithersburgh, Md., has licensed the BioWa Potelligent technology to develop therapeutic antibodies for potential therapeutic applications when enhancement of antibody-dependent cellular cytotoxicity is required.

Under the agreement, BioWa said it would provide MedImmune with non- exclusive commercial rights to use the technology to enhance ADCC in developing antibodies for multiple targets. In return, BioWa would receive technology access fees, and milestone payments and royalties on products developed by MedImmune, the company said.

* * *

Domantis Ltd. of Waltham, Mass., said it is entering into a multi-target discovery collaboration with **Bristol-Myers Squibb Co.** (NYSE: BMY) to develop dAb therapeutics for immunology and oncology.

The collaborators would discover dAbs as therapeutic targets in T-cell co-stimulation, the company said.

Under the agreement, Domantis said it would receive $9.2 million in upfront and guaranteed research payments. In addition, the company would be eligible for pre-clinical and clinical milestone payments of up to $20 million per product, as well as royalties on product sales. Domantis said it would contribute two of its dAb therapeutic programs and would create a range of dAbs to predetermined targets, with BMS having the exclusive right to develop and commercialize dAb therapeutics discovered during the collaboration.

* * *

Human Genome Sciences Inc. (Nasdaq: HGSI) of Rockville, Md., said it will spin off its **CoGenesys** division as an independent company that will develop early-stage selected gene-based product opportunities and the monetize Human Genome Sciences intellectual property and technology assets.

Under the agreement, HGS said it would provide CoGenesys with a start-up loan of $10 million to be repaid either in cash or equity at the option of HGS, following completion of CoGenesys funding. Human Genome Sciences will grant CoGenesys exclusive rights to develop and commercialize biological products based on human genes discovered by HGS, and will grant CoGenesys a license to use its proprietary albumin-fusion technology to develop and commercialize certain albumin-fusion proteins for therapeutic use.

HGS said it would have the right to retain an equity investment in CoGenesys, and would receive an upfront payment, either in cash or equity at the option of HGS, for the assets, intellectual property and technology licensed to CoGenesys. HGS also is entitled to a portion of the revenue CoGenesys receives from outlicensing or sales of therapeutic and diagnostic products successfully developed and commercialized, the company said.

HGS retains the right of first refusal prior to outlicensing by CoGenesys of several specific products that may be developed under the agreement. In addition, HGS has the option to have CoGenesys continue to perform pre-IND development work for up to two HGS products per year, with reimbursement for expenses on a cost-plus basis; CoGenesys will be entitled to milestone payments as any resulting products advance through development.

Craig Rosen, will join CoGenesys as executive chairman and chief scientific officer, and has resigned his posts as president, chief scientific officer and a director of Human Genome Sciences, the company said. Steven Mayer will join CoGenesys as CEO, and has resigned as executive vice president and chief financial officer. Both Rosen and Mayer will continue to serve as consultants to HGS.

Rosen and Mayer will be joined at CoGenesys by an early drug development team of 60 colleagues from HGS, including 20 Ph.D.-level scientists, the company said. Upon completion of funding, CoGenesys will become an independent company, and will assume salary and benefits obligations for its employees.

HGS products include HGS-ETR1 (mapatumumab) for non-small cell lung cancer, colorectal cancer and non-Hodgkin's lymphoma.

* * *

Lexicon Genetics Inc. (Nasdaq: LEXG) of The Woodlands, Tex., said it has expanded its drug discovery alliance with **Genentech Inc**. (NYSE: DNA) to include the advanced research, development and commercialization of biotherapeutic drugs.

Under the alliance, Lexicon would conduct advanced research on a subset of targets included in the Genentech Secreted Protein Discovery Initiative program and validated using the Lexicon proprietary gene knockout technology, the company said. Lexicon would develop and commercialize drugs modulating up to six of the targets. Genentech retains an option on the potential development and commercialization of the drugs under a cost and profit sharing arrangement, with Lexicon having certain conditional rights to co-promote drugs on a worldwide basis, the company said.

Lexicon said it would receive $25 million in upfront and milestone payments and research funding

during the three-year advanced research portion of the expanded alliance. In addition, Lexicon would receive payments from Genentech upon achievement of milestones related to the development and regulatory approval of drugs resulting from the alliance that are developed and commercialized by Genentech.

Lexicon is entitled to receive royalties on net sales of the products, provided they are not included in a cost and profit sharing arrangement. Genentech is entitled to receive milestone payments in the event of regulatory approval and royalties on net sales of products commercialized by Lexicon outside of a cost and profit sharing arrangement, the company said.

* * *

NanoMed Pharmaceuticals Inc. of Lexington, Ky., said that under an Inter-institutional Agreement with **Ohio State University**, the **University of Kentucky Research Foundation** has granted the company an option for an exclusive license to a Bioadhesive Berry Gel for the chemoprevention of oral epithelial dysplasia, the precancerous lesions of oral squamous cell carcinoma.

Researchers at Ohio, NanoMed and the UK Center for Pharmaceutical Science and Technology have been collaborating on the development of freeze-dried black raspberry gels for oral and topical cancer chemoprevention, the company said.

Freeze-dried black raspberries have been shown to inhibit the growth of several cancers in preclinical studies, the company said. Results from an open, phase I, multiple-dose pilot study in healthy volunteers showed that black raspberry extracts are well tolerated.

Russell Mumper, vice chair and associate professor in the University of Kentucky, College of Pharmacy and a co-founder of NanoMed PharmaceuticalsMumper, in collaboration with researchers at The Ohio State University and the James Cancer Hospital and Solove Research Institute, will evaluate the Bioadhesive Berry Gel in 20 patients with oral lesions in a phase I/Ia study, the company said.

The study is the chemotherapeutic efficacy of intraoral application of the Bioadhesive Berry Gel to induce regression, prevent recurrence, and inhibit progression in persons with oral epithelial dysplasia, the company said.

"As far as we know, there is no one anywhere else in the world using a bioadhesive gel like we are," said Susan Mallery, dentist and pathologist in The Ohio State University College of Dentistry and a member of The OSU Comprehensive Cancer Center, and part of the team investigating the product.

Clinical Trials:

Cell Therapeutics To Begin Trial Of Xyotax For NSCLC

(Continued from page 1)

favorable effect of estrogen on Xyotax metabolism," said Ramalingam.

Clinical data from a pooled analysis of the CTI STELLAR 3 and 4 trials in 198 women, demonstrated superior survival in those who received Xyotax (p=0.03), the company said. The most notable impact was among women younger than 55 and pre-menopausal who were treated with Xyotax compared to standard chemotherapy (median survival 10.0 vs. 5.3 months, hazard ratio=0.51, log rank p=0.038). While a survival trend (p=0.134) was observed in those 55 and older, the greater benefit observed among younger women is supportive of a positive impact of estrogen in Xyotax patients. Further support was observed in the STELLAR 3 trial, where blood estrogen levels were retrospectively analyzed. Women with higher estrogen levels, regardless of age, who were treated with Xyotax in combination with carboplatin had a significant improvement in overall survival compared to women treated with paclitaxel in combination with carboplatin (median survival 10.2 months vs. 5.5 months, hazard ratio=0.54, log rank p=0.039), the company said.

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

* * *

GlaxoSmithKline said it has begun a global multicenter phase II trial, the EGF105084 trial, to evaluate Tykerb (lapatinib) for ErbB2- overexpressing breast cancer that has metastasized to the brain.

Tykerb is an orally bioavailable small molecule that inhibits two receptors, ErbB2 and ErbB1, and is in development as a first-line treatment for ErbB2-overexpressing breast cancer, the company said.

The EGF105084 trial will enroll 220 patients for a more extensive analysis of safety and efficacy data in this setting, the company said. A similar population of patients was studied in an NCI-sponsored study in the Cancer Therapy Evaluation Program Trial 6969, and completed enrollment.

The EGF105084 trial would assess the impact of Tykerb therapy by monitoring lesions in the brain using magnetic resonance imaging, the company said. A centralized radiological review will be conducted and other treatment endpoints will include reduction in tumor-related neurological symptoms, duration of response to therapy, time to progression at any site and overall survival, the company said.

Study participants will be separated into two cohorts:

—One able to carry out most daily activities (ECOG Performance Status 0-1) and who have received one or two prior Herceptin-containing regimens.

—Patients ambulatory and capable of all self-care but unable to carry out any work activities, (ECOG Performance Status 2), or who have received more than two prior Herceptin-containing regimens.

* * *

GPC Biotech AG (Frankfurt Stock Exchange: GPC; TecDAX 30; Nasdaq: GPCB) of Martinsried and Munich said it has received clearance from the Paul-Ehrlich-Institut to begin a phase I trial of 1D09C3, an anticancer monoclonal antibody, for relapsed or refractory B-cell tumors where prior standard therapy has failed.

The open label trial is using a different dosing regimen from the phase I study underway in Switzerland and Italy, the company said. The study would determine the safety and tolerability of the antibody and recommend a dose and schedule for phase II studies. The second phase I study is being conducted at the University Hospital of Cologne under the direction of Michael Hallek, director of the Department of Internal Medicine.

1D09C3 is an anti-major histocompatibility complex class II monoclonal antibody that binds to MHC class II molecules on the cell surface and selectively kills activated, proliferating tumor cells, which include B-cell and T-cell lymphomas, the company said.

GPC Biotech has been granted orphan medicinal product designation for the treatment of Hodgkin's lymphoma by the European Medicines Agency.

In another development, GPC Biotech said it has achieved target enrollment in a phase III registration trial of Satraplatin, an orally bioavailable platinum-based compound, for second-line chemotherapy of hormone refractory prostate cancer

More than 200 clinical sites in 15 countries have accrued 912 patients to the Satraplatin and Prednisone Against Refractory Cancer, or SPARC trial, the company said. The trial is a multicenter, multinational, double blind, randomized study assessing the safety and efficacy of satraplatin in combination with prednisone as a second-line chemotherapy for hormone-refractory prostate cancer.

Phase II trials have been completed in HRPC, ovarian cancer and small cell lung cancer. A phase I/II trial of the agent combined with radiation therapy, for non-small cell lung cancer also has begun.

* * *

Kosan Biosciences Inc. (Nasdaq: KOSN) of Hayward, Calif., said it has begun a phase II trial for HER2-positive metastatic breast cancer, administering KOS-953 in combination with Herceptin (trastuzumab).

The phase Ib dose-escalating and phase II trials are being conducted at Memorial Sloan- Kettering Cancer Center and Arizona Cancer Center, the company said.

The phase II trial will enroll patients with HER2-positive metastatic breast cancer whose disease has progressed following treatment with trastuzumab in either the adjuvant or metastatic setting, the company said. Treatment will consist of weekly doses of KOS-953 following the infusion of trastuzumab. The primary objective is to assess tumor response using standard RECIST criteria.

The phase Ib trial was designed to determine the recommended phase II dose and toxicity of KOS-953 in combination with standard doses of trastuzumab, the company said. Standard weekly doses of trastuzumab followed by KOS-953 in escalating doses were administered. Ten patients received the final recommended phase II dose of KOS-953. Drug-related toxicities that were amenable to supportive care were gastrointestinal and fatigue. There was no marrow suppression and minimal hepatoxicity. No cardiovascular toxicity was observed. Pharmacokinetic parameters for KOS-953 in this combination were similar to KOS-953 administered as a single agent; KOS-953 had no effect on the kinetics of trastuzumab, the company said.

KOS-953 is a proprietary formulation of 17-AAG, an analog of the polyketide geldanamycin that inhibits heat shock protein 90, the company said. The Kosan geldanamycin analogs lead to the disruption of the Hsp90-client protein complexes and the degradation of the client proteins. One of the most sensitive client proteins is the HER2 receptor.

* * *

OXiGENE Inc. (Nasdaq: OXGN, XSSE: OXGN) of Waltham, Mass., said it would initiate a phase Ib trial of its vascular disrupting compound, Combretastatin A4 Phosphate.

The study would evaluate CA4P in combination

therapy with Avastin (bevacizumab), owned and marketed by Genentech (NYSE: DNA), the company said. Preclinical data showed that the combination of CA4P with the anti-angiogenic drug, Avastin, produced anti-tumor activity and could offer a highly targeted treatment strategy for solid tumors.

The trial with Avastin would be an open-label, multi-center study to determine the safety and tolerability of ascending doses of CA4P administered intravenously in combination with Avastin, the company said.

Dosing levels of CA4P would be escalated until a maximum tolerated dose is achieved. Anti-tumor effects and tumor response would be evaluated using the international standard for oncology clinical trials, Response Evaluation Criteria In Solid Tumors, or RECIST. Pharmacodynamic effects to assess blood flow shutdown to the tumor would be assessed with magnetic resonance imaging, the company said.

CA4P, a small-molecule drug candidate, is a vascular disrupting agent that causes vascular collapse and necrosis, the company said.

In a related development, **OXiGENE Inc.** said it has received regulatory clearance in the U.K. to begin a phase III trial of CA4P in combination with radiotherapy and chemotherapy for unresectable stage IIIb/IV non-small cell lung cancer.

The 370-patient study is a randomized, double blind, placebo-controlled trial where no prior treatment for NSCLC has occurred, the company said. The primary objective is to compare median survival time of the two groups. Tumor response will be evaluated using the international standard for oncology clinical trials, known as Response Evaluation Criteria In Solid Tumors, or RECIST.

The trial is designed to have a pre-planned, interim data analysis that will occur after half of the treatments are completed, to evaluate preliminary safety and response, the company said. The analysis will be performed by an independent third party review board that will establish whether the trial should proceed to its completion or be concluded for overwhelming efficacy, for safety concerns, or for futility.

The phase III trial has received approval from the Medicines and Healthcare Products Regulatory Agency in the U.K. and is subject to ethics approval by the Medical Research Advisory Committee, the company said. Clinical trial site selection is ongoing in the U.K. OXiGENE said it would file for regulatory clearance to add sites in other countries.

Interim data from the 2005 a phase Ib trial evaluating CA4P in combination with radiotherapy for NSCLC was presented at the NCI Cancer Conference in Birmingham, U.K, the company said. Data included two cohorts with NSCLC who received radiotherapy and either a single dose of CA4P at the end of the first week of radiotherapy treatment or once weekly doses of CA4P for three weeks. The cohort that received weekly CA4P for three weeks, as compared to the cohort that received a single dose of CA4P, showed a trend to increase the median survival to 11.6 months versus 6.8 months, respectively. Also, increased radiation toxicities had not been observed when CA4P was administered, and that the side effects of CA4P observed to date were mild and self-limiting, the company said.

* * *

Schering AG (FSE: SCH, NYSE: SHR) of Berlin said it has begun three phase II trials for cancers such as non-small cell lung cancer, ovarian cancer and breast cancer.

The studies will assess the safety and efficacy of the agent in each of the cancer types, the company said. The multi-center phase II study for recurrent ovarian cancer is being conducted in the U.K.

The metastatic breast cancer efficacy trial would enroll patients in 24 medical centers in Europe, with the first studies being initiated in France and Austria, the company said.

First clinical data from a phase I trial demonstrate that ZK-EPO exhibits favorable safety profile; anti-tumor activity in several solid tumors was also observed, the company said.

ZK-EPO is a fully synthetic epothilone, is microtubule stabilizer that accumulates preferentially in the nucleus of cells, the company said. It improves efficacy and safety compared to other chemotherapies and retains activity even in cancer cells that express the multi-drug resistant phenotype.

Also, the compound exhibits efficacy across a tumor models in vivo, including those resistant to widely used chemotherapeutic agents such as the taxanes and anthracyclines, the company said.

* * *

Spectrum Pharmaceuticals Inc. (Nasdaq: SPPI) of Irvine, Calif., said it has begun accrual in a phase II study of Satraplatin, in combination with Taxol (paclitaxel) as a first-line therapy for unresectable advanced non-small cell lung cancer.

The 40-patient phase II study for advanced NSCLC is an open label trial being led by investigators at the Sarah Cannon Research Institute in Nashville, the company said. The study also will be open for accrual in their affiliated network of oncologists, Tennessee

Oncology. The primary objective is objective response rate of satraplatin in combination with Taxol and to evaluate time to progression and overall survival.

The agent is in a phase III registrational trial as a second-line chemotherapy treatment for hormone-refractory prostate cancer, the company said.

* * *

Zila Inc. (Nasdaq: ZILA) of Phoenix said it has begun a phase III trial for OraTest, an oral cancer detection drug.

Zila said it reached an agreement with FDA under the Special Protocol Assessment process, on the design and size of the trial. The investigators received two days of intensive technical training specific to the protocol that will be followed.

The meeting provided training in an electronic data capturing system that will result in a timely review of enrollment progress, the company said. The 4,000 high risk-patient trial would require one visit, the company said. It would require one year for completion, once all investigator sites are active, but will include an interim analysis to determine the total number of patients required.

Product Approvals & Applications:

FDA Grants Priority Review For Sanofi's Taxotere sNDA

Sanofi-aventis Group (NYSE: SNY) of Bridgewater, N.J., said FDA has granted a six-month priority review for its sNDA for Taxotere (docetaxel) in combination with a current standard treatment, cisplatin and 5-fluorouracil, for advanced gastric cancer.

The application is based on data from a phase III international 457-patient study, TAX 325, for advanced gastric cancer, the company said.

Treatment with a Taxotere-based chemotherapy regimen, Taxotere, cisplatin and 5-fluorouracil, had an improved overall survival compared to standard treatment of cisplatin and 5-fluorouracil (9.2 months vs. 8.6 months median survival) with a relative risk reduction in mortality of 23 percent (log rank p=0.0201) and a 2-year survival of 18 percent versus 9 percent in favor of the Taxotere arm, the company said. In Europe, the supplemental application is under examination by the EMEA on the basis of the TAX 325 study results.

"If approved, the incorporation of Taxotere into a commonly used chemotherapy regimen may be the most important development in the treatment of advanced gastric cancer in more than a decade," said Jaffer Ajani, professor, GI medical oncology and principal investigator, M. D. Anderson Cancer Center.

In the study for locally advanced or metastatic gastric cancer, the primary study endpoint was time to tumor progression, the company said. This was improved with Taxotere based therapy (5.6 months) compared to standard treatment (3.7 months) with a 32 percent reduction in the risk of progression (log rank p=0.0004). The secondary endpoint was to detect a statistically significant increase in overall survival. Response rate, time to treatment failure, duration of response, safety profiles, QoL and disease related symptoms were collected and evaluated as secondary objectives as well, the company said.

The Taxotere combination resulted in an increased incidence of Grade 3-4 diarrhea (19 percent vs. 8 percent) and low white blood cell counts (82 percent vs. 57 percent) which was complicated by fever or infection in 29 vs. 12 percent of cases, the company said. In total, 81.4 percent of the patients experienced at least one grade 3-4 side effect with the Taxotere based regimen versus 75.4 percent in the control arm. And, there was a 57 percent reduction in Grade 3-4 neutropenia in patients who received G-CSF, the company said.

* * *

Halozyme Therapeutics Inc. (AMEX: HTI) of San Diego and **Baxter Healthcare Corp**. (NYSE: BAX) of Deerfield, Ill., said FDA has approved the Halozyme Hylenex recombinant, hyaluronidase human injection, as an adjuvant agent to increase the absorption and dispersion of other injected drugs.

Baxter would market and sell Hylenex, a proprietary recombinant human hyaluronidase, in the U.S., the companies said.

Results from a clinical trial conducted to support the Hylenex NDA demonstrated no allergic reactions to the agent and reduced injection site discomfort, the companies said. The double-blinded study compared Hylenex to a saline control in 100 volunteers. They were injected intradermally with Hylenex in one forearm and saline control in the other forearm, and evaluated for allergic responses and injection site side effects. The data showed injection site discomfort (e.g., stinging, burning, other discomfort) of 28 percent in the saline arm and 3 percent in the Hylenex arm, the company said.

Hylenex recombinant also is indicated for hypodermoclysis, and as an adjunct in subcutaneous urography for improving resorption of radiopaque agents, the company said. Hylenex recombinant is contraindicated in patients with hypersensitivity to hyaluronidase enzyme or any other ingredients in the formulation.

* * *

Novelos Therapeutics Inc. (OTCBB: NVLT) of Newton, Mass., said FDA agreed to advance NOV-002 into a single phase III study for advanced non-small cell lung cancer, in combination with first-line chemotherapy.

FDA concurred that a single well-controlled study would be sufficient to support licensure of NOV-002, in combination with chemotherapy, for the first-line treatment of chemotherapy-naive stage IIIb/IV NSCLC, the company said. Novelos said it would finalize the phase III study design under a special protocol assessment during the first half of next year.

The primary endpoint of the study would be overall survival, the company said.

NOV-002 is an oxidized glutathione-based compound. The drug has been approved in the Russian Federation where it was developed. The agent is designed to act as a chemoprotectant and an immunomodulator. It is marketed in Russia by Pharma BAM under the trade name Glutoxim.

NOV-002 also is being developed for chemotherapy-resistant ovarian cancer and acute radiation injury, the company said.

* * *

Varian Medical Systems Inc. (NYSE: VAR) of Palo Alto said it has received FDA clearance for an ocular cancer proton therapy treatment planning tool, part of its Eclipse radiotherapy treatment planning system.

The module allows the preparation of complex treatment plans to deliver proton radiation beams while protecting the eye, the company said.

Oncology Management:

Michigan BCBS To Expand Pilot Program In Breast Cancer

Blue Cross Blue Shield of Michigan and **Blue Care Network** said they will expand a pilot program to improve the quality of care in breast cancer.

The program will increase the number of participating Michigan hospitals from two to 17 over the next three years.

Working with the University of Michigan Health System, the Michigan Blues said they would invite five additional hospitals to participate in the new Michigan Breast Oncology Quality Initiative. Hospitals will be selected based on their volume of breast cancer cases, their past participation in the BCBSM Oncology Care Program—a collaborative effort to identify opportunities to improve cancer improvement care—and their commitment to tracking and providing data.

This is the fifth in a series of "collaborative quality initiatives" underway with sponsorship of the Michigan Blues in partnership with Michigan hospitals and physician groups. Other initiatives would assess and improve the quality of care in bariatric surgery, general and vascular surgery, cardiac and thoracic surgery, and cardiac angioplasty.

The breast cancer initiative began as a pilot project by researchers at two hospital systems, the University of Michigan Hospital and St. Joseph Mercy Hospital in Ann Arbor.

The data will be placed in a registry established by the National Comprehensive Cancer Network. Samuel Silver, professor of internal medicine at the University of Michigan Medical School and director of the University of Michigan Cancer Center Network, who led the pilot project, will direct the Michigan Breast Oncology Quality Initiative.

The project will bring together medical and surgical oncologists, radiation oncologists, radiologists and pathologists to examine patterns of care in their hospitals and practices, and compare them to NCCN practice guidelines, said Silver. Specific points of comparison will include the use of chemotherapy, hormonal therapy and sentinel node biopsy for early stage breast cancer.

About 7,000 women in Michigan are diagnosed with breast cancer every year.

* * *

Kinexus Bioinformatics Corp. of Vancouver said it has made available its first Internet accessible, cell signaling proteomics database, named KiNET, with built in bioinformatics searching capabilities.

KiNET, a functional proteomics database available to the health care research community, features over 200,000 measurements of the expression levels and phosphorylation states of hundreds of signal transduction proteins from hundreds of different biological specimens, including over 200 tumor cell lines, the company said.

The proteins tracked in KiNET are used for the operation of all cell and tissue types, as their malfunction has been linked to over 400 diseases including cancer, cardiovascular and neurodegenerative diseases, the company said. Clients are able to search KiNET to plan out a research project, discover drug targets and biomarkers for disease, or to better understand which pathways are regulated in response to various drugs and other treatments.