THE CANCER LETTER

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"Excitement" Building Toward 2015 Goal, NCI Director Says In FY07 Budget Request

By Kirsten Boyd Goldberg and Paul Goldberg

If Andrew von Eschenbach's introduction to the 2007 NCI "bypass" budget is to be believed, the war on cancer is going exceedingly well:

"Excitement continues to build across the cancer community about the progress we are making toward our Challenge Goal to eliminate the suffering and death due to cancer by 2015!"

Excitement is indeed in the air, but not of the sort the controversial NCI director and FDA acting commissioner would welcome. For the first time in his four years in Washington, von Eschenbach is encountering open resistance.

Directors of NCI-designated cancer centers are developing an "honest"

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In the Cancer Centers:

John Glick To Step Down After 21 Years Directing Penn's Abramson Cancer Center

JOHN GLICK, director of the Abramson Cancer Center of the University of Pennsylvania for the past 21 years, plans to step down on June 30. He plans to remain president and director of the Abramson Family Cancer Research Institute, continue his clinical practice in oncology, and work to increase philanthropic support for the center.

Since Glick's appointment in 1985, the center has grown from 120 to 300 members, with cancer research funding increasing from $10 million a year to more than $180 million a year. Its NCI Cancer Center Support Grant grew from $1.4 million in 1985 to $7.5 million this year. It ranks fifth in NCI cancer center funding.

"Anyone who knows John applauds his unwavering focus on the needs of patients and the vital role of Penn's Cancer Center to exceed those needs by delivering the most advanced treatments in a caring, compassionate environment," said Arthur Rubenstein, executive vice president, University of Pennsylvania and dean of the School of Medicine. "Since coming to Penn in 1974, John has devoted his tremendous energy to the betterment of Penn Medicine as a whole, setting a high standard for students, trainees, staff and colleagues alike."

Penn's Cancer Center wasn't recognized as a top center nationally and had little presence in the Philadelphia region 20 years ago, Glick said. Now, it's a model for a matrix-type center. With a $100-million commitment from Madlyn and Leonard Abramson, the university established the Abramson

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FY07 Bypass Budget Smallest In Three Years: $5.8 Billion

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alternative to his optimistic and ill-defined 2015 goal. Congress is challenging von Eschenbach on the conflicts of interest and commitment he faces as head of both NCI and FDA. The national press is applying a new level of scrutiny to von Eschenbach's conflicts, and cancer advocacy groups and professional societies have asked the White House to appoint "permanent qualified leadership" for the institute and the regulatory agency (The Cancer Letter, Nov. 23).

NCI's appropriations are expected to drop, and paylines for investigator-initiated grants are falling precipitously as von Eschenbach commits funds to speculative technology initiatives. All of this makes many oncology insiders wonder out loud whether this bypass budget will be von Eschenbach's last.

Three years ago, von Eschenbach defined his leadership of NCI around the 2015 goal, eliciting criticism and ridicule from mainstream scientists. Yet, he has not relented. Even after hearing criticism from cancer center directors in a private meeting last month, von Eschenbach only noted that "there were concerns among many that the timeline is too ambitious" (The Cancer Letter, Nov. 23).

The NCI bypass budget is a unique authority that stems from the National Cancer Act of 1971. Unlike other directors of NIH institutes, von Eschenbach can bypass review by NIH and the Department of Health and Human Services to ask the President and Congress for resources he needs to take advantage of scientific opportunities.

Smallest Request In Three Years

Von Eschenbach's latest bypass budget, released in November, opens with a response to naysayers. It is plastered in oversized letters on page 2, atop photos of smiling and presumably disease-free Americans: "Our Challenge Goal to the Nation: Eliminate the suffering and death due to cancer by 2015."

Great things will happen as a result of NCI's emphasis on technological tools, von Eschenbach promises. "Continued advances in high throughput computing, bioinformatics, imaging technology, nanotechnology, genomics, proteomics, and computational modeling are paving the way for new discovery and accelerated intervention development and delivery," he wrote in the introduction. "Collaborative efforts are streamlining the availability of tissue specimens, microarrays, image libraries, and epidemiological data."

Despite the aggressive goal, the bypass budget request is the smallest von Eschenbach has sought in three years—$5.889 billion for fiscal year 2007.

Indeed, the bypass budget requests have been shrinking. The FY07 request is $281 million less than last year's request of $6.17 billion. The previous year, NCI sought $6.2 billion for FY05, a slight increase over the FY04 request of $5.98 billion.

"Newly established partnerships with other agencies within the Department of Health and Human Services, with other Federal and state agencies, and with the private sector are helping us all to leverage limited resources and join together to ensure timely delivery of new cancer interventions to patients and people at risk," von Eschenbach wrote. "We have enormous responsibility in a time when resources are more precious than ever."

NCI's FY05 budget was $4.8 billion. Congress hasn't finalized the budget for FY06, which began Oct. 1. At this writing, cancer groups are lobbying Congress to exempt NIH from across-the-board budget cuts.

The latest bypass budget seeks an increase of $291 million to maintain "current services." About half of this increase, $146 million, would go toward research project grants.

In addition to the current services increase, NCI seeks about $800 million in new funding for five "new strategic investments." These represent "a critical path for reaching NCI's Challenge Goal to the Nation," the

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document states. "Each promises to yield high return but will require a substantial investment of resources."

These include:

—Expanding cancer center reach: $164 million. NCI proposes to add 15 new cancer centers over the next five years and support more community outreach.

—Reengineering clinical trials: $171 million. The funds would support the implementation of the Clinical Trials Working Group recommendations to improve clinical trials coordination, prioritization, and standardization.

—Linking science and technology: $194.8 million. Funds would support new imaging technologies, nanotechnology, genomics, proteomics, biomarker discovery, and computational modeling.

—Advancing medical informatics: $80 million. Among the proposals is an expansion of the Cancer Bioinformatics Grid, support for research and innovation on electronic medical records, and development of software applications to expand the use of electronic pathology records in combination with cancer incidence data.

—Integrating cancer science: $190 million. Funds would support research that takes a "systems biology" approach to cancer or integrates "the biological with the population and public health sciences." Also included is support for advanced technologies and translational research.

Everyone Must "Do Their Part"

The plan will work if everyone works together, von Eschenbach wrote.

"We as a Nation will succeed when everyone works in close harmony to relay cancer information and ensure the adoption of evidence-based interventions," von Eschenbach wrote in his introduction. "We must help all of our citizens maintain healthy lifestyles, get screened regularly, obtain prompt treatment when cancer is diagnosed, and have access to quality follow-up care.

"Researchers across many disciplines, technology experts, public health specialists, healthcare providers, patients, people at risk, and healthy people must work to define and do their part. People all over the world demonstrate their ability to overcome the odds every day. Cancer will be no exception."

"The Nation's Investment in Cancer Research: A Plan and Budget Proposal for Fiscal Year 2007" is available online at http://plan.cancer.gov. Print copies may be ordered by sending an e-mail to ci-socc@pop.nci.nih.gov.

Capitol Hill:

Bill Would Allow Drug Sales After Phase I Trial Completion

By Paul Goldberg

Cancer groups are maintaining silence on a month-old Senate proposal to change the drug approval process to allow companies to sell treatments for catastrophic diseases after completion of phase I trials.

The legislation was developed by Sen. Sam Brownback (R-Kan.), based on a plan by the Abigail Alliance for Better Access to Developmental Drugs. Brownback introduced the bill on Nov. 3.

Patient advocacy groups and professional societies that advocate for rigorous drug approval criteria say they are watching with interest whether the bill—S. 1956, Access, Compassion, Care and Ethics for Seriously-Ill Patients Act—has any chance of advancing.

The bill, which has one co-sponsor, Sen. James Inhofe (R-Okla.), and no House version, represents a consensus that has developed in conservative think tanks, as well as some patient groups and some quarters of the pharmaceutical industry.

Steven Walker, an advisor to the Abigail Alliance and the author of its "Tier I" proposal, said the bill translates his regulatory vision into legislative language. "We support the bill," he said.

Proponents and critics alike are unable to read the administration's position on the measure. However, the bill is largely consistent with the vision laid out by FDA Acting Commissioner and NCI Director Andrew von Eschenbach, who has spent the past four years at the institute describing plans for accelerating cancer research, lowering reliance on randomized trials, and making greater use of surrogate endpoints for prevention and treatment of cancer.

After he was named to the top job at FDA, von Eschenbach said he would "streamline and accelerate" the drug approval process. Later, he said FDA would join the pursuit of his goal to end "suffering and death due to cancer" by 2015 (The Cancer Letter, Oct. 7, Oct. 21).

Brownback is a co-chairman of the Senate Cancer Coalition. The other co-chairman, Sen. Dianne Feinstein (D-Calif.), who is also the vice chairman of C-Change, hasn't co-sponsored the measure.

The bill would limit the companies' ability to conduct placebo-controlled trials, which have become more feasible with oral treatments for cancer, and would institute Tier I approval that would allow companies to charge for drugs that have gone through phase I testing.

Brownback's bill drew applause from The Wall Street Journal editorial writers, who have spent two decades campaigning against randomized trials and the FDA requirement that drugs demonstrate efficacy before they can be approved (The Cancer Letter, Aug. 5).

"The logic here is that if drugs have shown themselves safe and effective enough in so-called phase I trials for FDA to approve giving them to hundreds or thousands of patients on phase II studies, there is no good reason to withhold them from a broader patient population that has run out of other options," the Journal wrote Nov. 15.

The editorial writers appear to be taking a chance that an average reader wouldn't know that phase I trials aren't designed to measure efficacy.

In a statement, Brownback said his goal is to get bureaucrats off the backs of dying patients. "The decision for terminally ill patients to take an investigational drug should be between the physician and patients, not government bureaucrats," he said.

However, Brownback, the Journal, and Abigail Alliance are also attacking a bigger target: the need for randomized trials as a basis for drug approval. The bill, which has been referred to the Senate Committee on Health, Education, Labor, and Pensions, calls for a fundamental overhaul of the drug approval process.

Three Tiers of Approval

Approval of therapies for catastrophic illnesses would be divided into three "tiers."

The first tier of approval would allow companies to sell drugs based on "information from completed Phase I clinical investigations and any other non-clinical or clinical investigations."

According to the bill, "Tier I approval shall be primarily based upon clinical evaluation, not statistical analysis." Admissible evidence would include "uncontrolled data such as case histories, information about the pharmacological mechanism of action, data from animal and computer models, comparison with historical data, or other preliminary information, and may be based on a small number of patients."

FDA would be required to either approve the application within 30 days or to refer it to a proposed "Accelerated Approval Advisory Committee." To receive treatment, patients would be obligated to sign releases from liability should adverse events occur.

The next tier of approval would be granted based on "data and information that the drug, biological product, or device has an effect on a clinical endpoint or on a surrogate endpoint or biomarker that is reasonably likely to predict clinical benefit to a patient (who may be representative of a small patient subpopulation) suffering from a serious or life-threatening condition or disease."

According to the bill, a sponsor "may be subject to the requirement that the sponsor conduct appropriate post-approval studies to validate the surrogate endpoint or biomarker or otherwise confirm the effect on the clinical endpoint."

Companies would be allowed to promote therapies approved under Tier I or II programs, provided they "submit copies of all advertising and promotional materials related to the product."

Approval could be withdrawn if a sponsor "fails to conduct post-approval studies with due diligence," if a post-approval study "fails to verify clinical benefit of the product for even a small patient subpopulation," or if "other evidence demonstrates that the product is not safe or effective under the conditions of use for even a small patient subpopulation."

A Ban on Placebo?

The bill would make it illegal for companies to conduct placebo-controlled trials.

"The Secretary shall prohibit placebo-only or no-treatment-only concurrent controls in any clinical investigation conducted under this chapter or, in the use of the last-observation-carried-forward convention, in any clinical investigation… with respect to any life-threatening condition or disease where reasonably effective approved alternative therapies exist for the specific indication."

Also, the HHS secretary would be mandated to encourage development of drugs based on surrogate endpoints:

—"Establish a program to encourage the development of surrogate endpoints and biomarkers that are reasonably likely to predict clinical benefit for serious or life-threatening conditions for which there exist significant unmet medical needs;"

—"Request the Institute of Medicine to undertake a study to identify validated surrogate endpoints and biomarkers, and recommend research to validate surrogate endpoints and biomarkers, that may support approvals for products intended for the treatment of serious or life-threatening conditions or diseases;

—"Make widely available to the public a list of drugs, biological products, and devices that are being investigated for serious or life-threatening conditions or diseases and that have not yet received Tier I or Tier II approval for marketing."

"Non-Statistical Measures"

The bill makes it illegal for FDA to withhold approval based solely on a therapy's failure to meet a statistically defined endpoint.

The measure states:

"The Secretary shall give equal weight to clinical judgment and statistical analysis in the evaluation of the safety and effectiveness of drugs, biological products, and devices, and shall not disapprove a product application solely on the basis of a statistical analysis or the rigid use of the 95 percent confidence level convention.

"This policy shall apply in evaluating clinical study designs and endpoints; and in making decisions with respect to product applications."

"Non-statistical" measures would include:

—"clinical evaluation information, such as case history reports;

—"scientific and clinical studies designed to measure or define mechanisms of action or molecular targeting;

—"data from animal and computer models; and

—"comparison with historical data; and

—"shall incorporate the use of evaluations of the adverse effect of delaying the availability of an investigational drug to even a small subpopulation of seriously ill patients; and scientific, observational, or clinical studies designed and conducted to collect well-documented information."

Kidney Cancer Patient Responds

Responding to the Journal editorial, Bill Bro, CEO of the Kidney Cancer Association said scientists and ethicists are divided on the subject of placebo-controlled trials.

"While a few researchers make ethical objections to placebo controls, there is no consensus on this controversial issue," he wrote in a letter submitted to the Journal. "Many respectable investigators, including nationally-recognized oncologists who serve on our organization's medical board, argue that such controls are essential to the responsible and swift approval of new cancer drugs…

"Once again, The Wall Street Journal has dealt with this sensitive issue in an inflammatory manner," Bro wrote. "Why not instead attempt to better inform the public about the complexity of the drug approval process?

"If clinical trials fail to accrue sufficient numbers of patients, many useful cancer-fighting drugs will never get into the marketplace. This is the issue that deserves widespread publicity—and it is critically important to research in rare and deadly cancers."

The Journal hasn't published Bro's letter.

NCI Programs:

NCI Advisors Approve Plans For New, Renewal RFAs

By Kirsten Boyd Goldberg

NCI's Board of Scientific Advisors recently approved the institute's plans to issue seven Requests for Applications for a variety of new and existing programs.

The concepts approved at the board's Nov. 14 meeting included:

—Increasing the Utilization and Impact of the Cancer Information Service, approved on a vote of 19-3.

—Tumor Microenvironment Consortium, unanimous approval.

—Alliance of Glycobiologists for Detection of Cancer and Cancer Risk, approved 13-9.

—Minority Institution Cancer Center Partnership, consisting of three RFAs, approved 16-0 with five abstentions.

—Supplements for Image-Guided Interventions in SPOREs, unanimous approval.

Excerpts from NCI's concept statements describing the grant programs follow:

Increasing the Utilization and Impact of the National Cancer Institute's Cancer Information Service. Concept for a new RFA, first-year set-aside $1.3 million, total $2.6 million over two years, six to seven R21 grants. Program directors: Linda Squiers and Bradford Hesse, Division of Cancer Control and Population Sciences and NCI Office of Communications.

The R21 will support studies that explore the development and testing of national, regional, or community-based interventions that increase the utilization of the Cancer Information Service by the underserved as well as the impact of the information and education delivered by the CIS. For this RFA, underserved populations are defined as those who experience social inequities.

The purpose of this RFA is to stimulate research that explores effective messages, channels, outreach, promotional strategies, or other interventions that increase the utilization and impact of the CIS by underserved populations. Of special interest is formative research that explores how to engage health care providers, especially those serving the underserved populations, in using and referring patients to the CIS for relevant prevention, screening, treatment, and survivorship information and educations. In addition, studies that test the delivery of strategies that connect underserved

populations to the CIS through established organizations or networks are desired. The research should be conducted in collaboration with at least one CIS contractor/regional office. An information packet will be available to investigators that identifies the location and contact information for each of the regional offices as well as descriptions of each of the program components offered by each of the 15 regional offices that hold CIS contracts. When feasible, investigators should use current surveillance and service data to plan and assess study outcomes.

Tumor Microenvironment Consortium. Concept for a new RFA, first-year set-aside $12 million, total $60 million over five years, six U01 awards. Program director: Suresh Mohla, Division of Cancer Biology.

The objective of this initiative is to delineate mechanisms of tumor stromal interactions in human cancer. Such an effort is likely to generate a comprehensive understanding of stromal composition in normal tissues and its role in tumor initiation, progression, and metastasis. This initiative is intended to support a network of up to six individual programs, each consisting of multi-disciplinary teams of investigators with expertise in specific tumor sites and using human cancer samples or well-credentialed vertebrate models. Individual programs funded under this initiative are expected to focus on defined and biology-driven research projects and are expected to address one or more of the following major scientific areas: a) delineating the role of tumor stromal interactions in cancer, which may require characterization of stromal cells, b) delineating the role of inflammatory and other immune cells in tumor initiation and progression, and c) identification of tumor stem cells and/or other relevant stem cells within the stroma and delineation of their interactions with stromal cells. Members of the consortium would also be expected participate in collaborative efforts developed within the consortium that are directed at developing critical resources and reagents, and developing novel technologies, and outreach activities to ensure dissemination of such resources and technologies to the broader research community.

The total cost of each program funded would be limited to $1.83 million per year for five years.

Alliance of Glycobiologists for Detection of Cancer and Cancer Risk. Concept for a new RFA, first-year set-aside $3 million, total $15.8 million over five years, up to six awards. Program directors: Sudhir Srivastava and Karl Krueger, Division of Cancer Prevention.

The primary objective of this initiative is to solicit applications focused on the discovery and development of glycomics-based cancer biomarkers for early detection. A secondary objective is to bring in a new cadre of investigators, particularly among carbohydrate chemists, glycobiologists, and other related specialists.

In partnership with the NIGMS-supported Consortium for Functional Glycomics, which will make available a menu of resources and services, this initiative seeks to capitalize on the great potential the field of glycomics offers for cancer diagnostics. In response to this initiative, investigators may propose to identify unique glycans from a large number of organ sites and then to evaluate the utility of these glycans for identifying early cancer or cancer risk. Three specific areas encouraged, but not restricted by this initiative are:

1. Identify oligosaccharide-based biomarkers specific to defined tumors that can be used for early detection, diagnosis, prognosis, or monitor response to therapy.

2. Development and application of glycan arrays for cancer biomarker discovery and validation and screening.

3. Development and validation of additional tools and reagents to enable high-throughput testing of glycomic biomarkers.

Applicants are expected to assemble a team of investigators prior to submitting their application; this team will form the nucleus of their Tumor Glycome Laboratory. The necessary expertise is expected to include glycobiologists to support continued development and adaptation of the selected technologies; basic cancer researchers; and oncologists and pathologists to provide the cancer expertise that will ensure the selection of appropriate specimens for analysis.

The U01 mechanism will support four to six projects for up to five years; $3 million is requested for the first year: $2.5 million for Tumor Glycome Laboratories; $500,000 for reagents and arrays (to be procured from CFG) and $3.2 million for subsequent years; and additional $200,000 is defrayed costs for data analysis and tools development in collaboration with the Early Detection Research Network Data Management Coordinating Center and the NCI Center for Bioinformatics.

Minority Institution Cancer Center Partnerships. Comprehensive Minority Biomedical Branch, Office of Centers, Training, and Resources. Re-issuance of three RFAs:

—Feasibility Studies for Collaborative Interaction for Minority Institution/Cancer Center Partnership (P20), first-year set-aside $1.2 million, total $4.8 million over four years, six awards.

—Cooperative Planning Grant for Comprehensive Minority Institution/Cancer Center Partnership (U56), first-year set-aside $800,000, total $4 million over five years, two awards.

—Comprehensive Minority Institution/Cancer Center Partnership (U54), first-year set-aside $3.5 million, total $17.5 million over five years, two awards.

This program asks minority-serving institutions and NCI-designated cancer centers to combine their expertise to produce more competitive grant funding from minority investigators in cancer research, training education and outreach; enhance the competitive research capacity at MSIs; increase cancer outreach from cancer centers in minority communities; and augment research at cancer centers directed at cancers that disproportionately affect and burden racial, ethnic minority, and underserved populations.

Since the program began in 2001, a total of 67 awards have been made including 34 P20s, 20 U56s, and 13 U54s.

The MI/CCPs target four areas, of which the U56 and U54 partnership proposals must include research and training, and either education or outreach. The P20 partnership proposals must include research and either training or education. Outreach is not a requirement of the P20s.

1. Cancer research: Joint pilot research projects may be in any area of basic, clinical, prevention, control, behavioral, or population research. Research projects conducted primarily at the MSI may be in any area of cancer research, but research projects conducted primarily at the cancer center must specifically address areas of cancer disparity in minority or underserved populations. The expectation is that successful pilot projects will become full research projects and will become competitively funded grants.

2. Cancer training: Cancer training is the most productive way to sustain a long-term effective partnership. These programs must place an emphasis on the training of minority scientists and on educating minority investigators and trainees to appreciate the issues and problems associated with cancer disparities in minority populations. NCI particularly encourages training of minority scientists in basic, clinical, behavioral, and population research.

3. Cancer education: Cancer education programs could focus on any effort to augment existing or create new curricula in the MSI and/or the cancer center. These programs would apprise and culturally sensitize graduate, postdoctoral, and medical students in research, medicine, and public health of the need to reduce cancer health disparities in minority and underserved populations.

4. Cancer outreach: Cancer outreach programs may be defined as proactive efforts to help minority communities develop and manage their own culturally sensitive programs for educating their populations about cancer risk, early detection, screening, prevention, and treatment.

Supplements for Image-Guided Interventions in SPOREs. Concept for reissuance of an RFA, first-year set-aside $1 million, total $2 million over two years, four awards. Cancer Imaging Program director Keyvan Farahani, Division of Cancer Treatment and Diagnosis.

This is a request to re-issue a Letter RFA to provide administrative supplements to SPOREs and cancer centers for translational research in Oncologic image-guided interventions (IGI). The original FY05 Letter RFA was issued in December 2004; 53 two-year project applications were received by the June 1, 2005, receipt date.

In the evaluation process, 37 of the 53 (70%) of applications were found to be responsive. Although many were meritorious, available funds enabled only four awards, for a total of $1.07 million in FY05. The overwhelming response demonstrated a great breadth and depth of interest and developmental activity in IGI. At the same time, it indicated a clear need to further boost translation by investing additional resources in this burgeoning area of new minimally-invasive cancer treatments.

Image-guided interventions in oncology include regional and local therapies, guided by real-time imaging, with the common aim of tumor destruction. IGIs reduce or eliminate tumor burden by minimally invasive means, to achieve clinical objectives, which range from palliation to cure, but which always include improved quality of life. IGI procedures are performed non-invasively, minimally-invasively, or intraoperatively.

For this award, pre-treatment imaging for diagnostic or planning purposes does not qualify as IGI or a component of IGI, unless the image data is integrated into the actual procedure. Also, the imaging component of the research must be in vivo imaging.

This initiative will encourage partnering between investigators of the SPOREs and cancer centers ad their basic science and engineering colleagues, within and outside of the institution, and industry, when appropriate. This initiative will encourage industry-academic partnerships so as to leverage the available funds and to maximize the eventual translation of strategies developed to all medical centers. It will encourage interactions with Cancer Centers for Nanotechnology Excellence to further explore the use of nanodevices in image-guided oncologic interventions.

Funding Opportunities:
NIH Director's Pioneer Award

Applications Receipt Dates: Between Jan. 15 and Feb. 27, 2006. The award allows individual scientists Unlike other NIH grants, which support research projects, the Pioneer Award supports, allowing them to pursue new research directions and innovative ideas. The program is open to scientists at all career levels. The scientists may be working in any field of research provided they are interested in exploring biomedically relevant topics and willing to commit the major portion of their effort to Pioneer Award research. Awardees must be U.S. citizens, non-citizen nationals, or permanent residents. Applications are available at http://grants1.nih.gov/grants/guide/rfa-files/RFA-RM-06-005.html.

Program Announcements

PA-06-055: Bioengineering Approaches to Energy Balance and Obesity

The PA would support bioengineering technology that examines clinical problems related to energy balance, intake, and expenditure. Novel sensors, devices, imaging, and other approaches are expected to be developed and evaluated by collaborating engineers, physical scientists, and scientists from other relevant disciplines with expertise in obesity and nutrition. The goal is to increase the number of useful technologies and tools available to scientists to facilitate their research in energy balance and health that would facilitate therapeutic advances and behavioral changes for weight control and obesity. The PA would use the SBIR R43/44 funding mechanism. The PA is available at http://grants.nih.

gov/grants/guide/pa-files/PA-06-055.html

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PA-06-056: Bioengineering Approaches to Energy Balance and Obesity. The PA would use the SBIR R41/42 funding mechanism. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-06-056.html.

PA-06-031 Image-Guided Cancer Interventions. The PA supports the development and clinical validation of systems for image-guided interventions for cancer. The program would development and optimization of fully integrated cancer imaging, monitoring, and therapy systems; the validation of integrated IGI systems through clinical evaluations; the development of multiple prototype integrated IGI systems as required for multi-site clinical evaluations; and partnerships among small business, large business, and academic clinical centers, as well as small business joint ventures, in order to reach the research goal. The PA will use the STTR R41/R42 grant mechanism. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-06-031.html

Inquiries: For NCI--Keyvan Farahani, 301-496-9531; farahank@mail.nih.gov. Laurence Clarke, 301-435-9190; lclarke@mail.nih.gov.

PA-06-032: An SBIR Initiative for Image-Guided Cancer Interventions. The PA will use the SBIR R43/R44 grant mechanisms. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-06-032.html.

In the Cancer Centers:

Penn To Begin Director Search

(Continued from page 1)

Family Cancer Research Institute in 1997. "This allowed an unprecedented expansion of cancer research at Penn, culminating in the recruitment of **Craig Thompson** as scientific director," Glick wrote in a memo to center members. "In the years 1999-2004, a total of 90 new faculty were jointly recruited to many Penn departments and the cancer center. It is our faculty who deserve the collective credit for making the cancer center a living, breathing entity."

Rubenstein said the university will begin a search for a new center director soon. "Whoever is selected will be the beneficiary of a life's work exceedingly well done," he said.

* * *

M. D. ANDERSON CANCER CENTER and **Fudan University Cancer Hospital** in Shanghai were awarded a four-year $2.15 million grant from NCI to expand studies of traditional Chinese medicine in cancer treatment. **Lorenzo Cohen** is principal investigator and director of the Integrative Medicine Program at M. D. Anderson. The co-principal investigator at Fudan University Cancer Hospital is **Liuming Liu**, and the co-director is **Zhiqiang Meng**. . . . **JOHN H. JARDINE** Center for Veterinary Medicine and Surgery was dedicated at M.D. Anderson Nov. 16. Jardine, who died in 1997, was the first veterinarian at M. D. Anderson when he joined the staff in 1962. The 55,000-square-foot center is located in the basement of the M. D. Anderson Clinical Research Building. . . . **GARTH POWIS** was named chairman of the Department of Experimental Therapeutics and director of the Center for Targeted Therapy at the new Red and Charline McCombs Institute for the Early Detection and Treatment of Cancer at M. D. Anderson. Powis was a professor of pathology and pharmacology at the University of Arizona and director of basic research for the Arizona Comprehensive Cancer Center. . . . **MONICA MORROW**, chairman of the Department of Surgical Oncology at Fox Chase Cancer Center, was elected a fellow of the Royal College of Physicians and Surgeons of Glasgow. . . . **BARBARA NICHOLSON** was named associate director for special initiatives at Vanderbilt-Ingram Cancer Center. She will lead projects for the cancer center director including relationship management and support for the Board of Overseers. Most recently, she was director of the capital campaign for the Nashville Hope Lodge that provides housing for cancer patients.

NCI Mouse Genetics Leaders Copeland, Jenkins Plan Move

NCI GENETICISTS Neal Copeland and **Nancy Jenkins**, leaders of the Mouse Cancer Genetics Program, plan to leave the institute next year to join Singapore's Institute of Molecular and Cellular Biology.

The senior investigators—Copeland heads the Molecular Genetics of Oncogenesis Section and Jenkins heads the Molecular Genetics of Development Section—have coauthored nearly 700 publications since moving to NCI-Frederick in 1985. They were among the first to develop a detailed molecular genetic linkage map of the mouse genome.

Even after moving to Singapore, Copeland and Jenkins plan to continue to help run the NCI program as "special volunteers," Copeland said. Their reasons for leaving include the institute's tight intramural research budget and new ethics rules limiting consulting arrangements, he said.

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Business & Regulatory Report

Product Approvals & Applications:

FDA Approves Tarceva Plus Gemcitabine For Advanced Pancreatic Cancer

OSI Pharmaceuticals Inc. (Nasdaq: OSIP) of Melville, N.Y., and **Genentech Inc.** (NYSE: DNA) of South San Francisco said FDA has approved Tarceva (erlotinib) in combination with gemcitabine for advanced pancreatic cancer with no prior chemotherapy treatment.

Tarceva showed a statistically significant improvement in overall survival when added to gemcitabine chemotherapy as initial treatment for pancreatic cancer in a phase III study, the company said.

The treatment is a once-daily oral tablet already approved for non-

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Clinical Trials:

Coley Begins Phase III Studies of Therapy For NSCLC; Idera Begins Phase I/II Trial

Coley Pharmaceutical Group Inc. (Nasdaq: COLY) of Wellesley, Mass., said it has begun two phase III studies of PF-3512676, CPG 7909, formerly ProMune, for first-line non-small cell lung cancer under the special protocol assessment procedure of FDA.

The phase III program, begun by Coley's partner Pfizer Inc., will evaluate PF-3512676 in combination with standard chemotherapy regimens versus chemotherapy alone in the first-line treatment for advanced non-small cell lung cancer, the company said. The primary endpoint is overall survival. Each of the trials will enroll 800 adults with stage IIIb or IV disease, the company said.

PF-3512676, a Toll-like receptor 9 agonist, is delivered by subcutaneous injection, the company said.

Coley said it conducted a multi-center phase II study of 112 patients in which results indicated a meaningful patient survival benefit among those receiving PF-3512676 in combination with chemotherapy versus those who received chemotherapy alone for the first-line treatment of both of the major histologic subtypes of non-small cell lung cancer.

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Idera Pharmaceuticals Inc. (AMEX: IDP) of Cambridge, Mass., said it has begun a phase I/II trial of HYB2055 in combination with gemcitabine and carboplatin for advanced non-small cell lung cancer.

The trial is open to enrollment at Lombardi Comprehensive Cancer Center at Georgetown University Medical Center, the company said.

HYB2055, also known as IMO-2055 or IMOxine, is a Toll-like Receptor 9 agonist based on the Idera proprietary Immune Modulatory

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small cell lung cancer where the disease has progressed after one or more courses of chemotherapy. OSI also announced that Roche, its international partner for Tarceva, has submitted a marketing authorization application to the European Health Authorities for pancreatic cancer.

"Improvements in therapy in advanced pancreatic cancer have been very difficult to come by," said Malcolm Moore, study chairman and medical oncologist at Princess Margaret Hospital in Toronto, and chairman of the Gastrointestinal Disease Site, National Cancer Institute of Canada Clinical Trials Group. "As a molecularly targeted agent, erlotinib has been shown to add a survival benefit when combined with gemcitabine for patients facing pancreatic cancer."

The FDA based the approval decision for Tarceva on results from a randomized double-blind, placebo-controlled phase III study of the treatment in combination with gemcitabine chemotherapy for unresectable locally advanced or metastatic pancreatic cancer. The global study, which was conducted by NCI in collaboration with OSI Pharmaceuticals, met its primary endpoint of improving overall survival.

Compared to gemcitabine plus placebo, those receiving gemcitabine plus Tarceva 100 mg/day demonstrated a statistically significant (23 percent) improvement in overall survival (hazard ratio = 0.81; p = 0.028), the company said.

After one year, 24 percent receiving Tarceva plus gemcitabine were alive compared to 19 percent receiving gemcitabine plus placebo, the company said. A statistically significant improvement in progression-free survival (hazard ratio = 0.76; p = 0.006) also was demonstrated. Although no difference in tumor response was observed (8.6 percent in those receiving Tarceva plus gemcitabine versus 7.9 percent in the gemcitabine plus placebo arm), the disease control rate (complete response + partial response + stable disease) was significantly improved (59 percent in patients receiving Tarceva plus gemcitabine versus 49 percent in the gemcitabine plus placebo arm, p = 0.036).

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AstraZeneca (NYSE: AZN) of Wilmington, Del., said FDA has granted orphan-drug designation for Zactima (ZD6474) for follicular, medullary, anaplastic, and locally advanced and metastatic papillary thyroid cancer.

The agent is designed to be a multitargeted compound, directed to the inhibition of cell signaling pathways in tumor growth and spread, the company said. Tumor cells are targeted through inhibition of epidermal growth factor receptor and RET tyrosine kinases, while tumor blood supply is targeted through inhibition of vascular endothelial growth factor receptor tyrosine kinase.

Zactima is in phase II trials in medullary thyroid cancer and phase III trials in advanced non-small-cell lung cancer, the company said.

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Celgene Corp. (Nasdaq: CELG) of Summit, N.J., said the European Medicines Agency has accepted for review its marketing authorization application for Revlimid (lenalidomide).

The application is based phase II trial data of the agent for myelodysplastic syndromes with deletion 5q chromosomal abnormality, the company said. Celgene said it is seeking authorization to market the product for transfusion-dependent anemia due to low- or intermediate-risk MDS associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.

Revlimid has been designated an Orphan Medicinal Product in the European Union for MDS and multiple myeloma, the company said. Celgene said it would file its supplemental NDA and MAA with FDA for previously treated patients who are relapsed and refractory.

In another development, Celgene said FDA has

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issued an approvable letter in response to the sNDA for Thalimid (thalidomide) multiple myeloma.

FDA has requested revised product labeling with the specific indication of newly diagnosed multiple myeloma and updated safety information, the company said.

The Thalomid sNDA is based on data from a large phase III randomized Eastern Cooperative Oncology Group study comparing thalidomide plus dexamethasone to dexamethasone alone for untreated multiple myeloma.

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Dendreon Corp. (Nasdaq: DNDN) of Seattle said FDA has granted Fast Track review status to Provenge, sipuleucel-T, for asymptomatic metastatic, androgen-independent prostate cancer.

Data from a phase III study, D9901, and supporting data from study D9902A, showed a survival benefit, the company said. Dendreon said it can now submit a U.S. biologics license application on a rolling basis, which permits FDA to review sections of the BLA in advance of receiving the complete submission.

Provenge, an active cellular immunotherapy, stimulates the immune system, the company said. The drug targets the prostate cancer antigen, prostatic acid phosphatase, which is found in approximately 95 percent of prostate cancers. In clinical studies, three infusions were administered over a one-month period as a complete course of therapy, the company said.

In a related development, Dendreon said it has reached an agreement with FDA under the Special Protocol Assessment procedure to amend the design of its phase III, D9902B, trial of Provenge, sipuleucel-T, an investigational active cellular immunotherapy for advanced prostate cancer.

The SPA letter is a written agreement between Dendreon and the FDA on trial design and outlines clinical objectives and data analyses, the company said.

The D9902B trial began in June 2003 under a SPA for asymptomatic, metastatic, androgen-independent prostate cancer where tumors had been classified with a Gleason score of 7 or lower, the company said. Based on data from two completed phase III studies of Provenge, D9901 and D9902A, the company has amended the D9902B protocol, which will now be known as the IMmunotherapy for Prostate AdenoCarcinoma Treatment, or IMPACT study.

Amendments to the study include the following: Enrollment will no longer depend on Gleason Score; those with minimally symptomatic disease-related pain will be eligible; the primary endpoint of the study is now overall survival, which will be an event-driven analysis, and time to objective disease progression is now a secondary endpoint; the trial is designed to enroll approximately 500 men in the study; and the primary statistical analysis to determine efficacy will be the Cox multivariate regression model. The same Cox model was used to analyze overall survival in the D9901 and D9902A studies, the company said.

Dendreon recently held a pre-BLA meeting with FDA to review safety and efficacy data from its two completed phase III clinical trials of Provenge, D9901 and D9902A, in men with asymptomatic, metastatic, advanced prostate cancer.

"The amendment to the IMPACT study protocol should enable us to expedite enrollment would provide all qualified patients access to Provenge while we complete the BLA submission process," said Robert Hershberg, chief medical officer at Dendreon. "The trial could provide us with an opportunity for an expanded label for minimally symptomatic disease."

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EntreMed Inc. (Nasdaq: ENMD) of Rockville, Md., said FDA has accepted its IND application for ENMD-1198, a tubulin-binding agent.

Phase I studies would begin next year, the company said. ENMD-1198 is based on a modified chemical structure of 2ME2 designed to increase antitumor and antiangiogenic properties and improve metabolism. The agent is characterized by its multiple mechanisms of action, which include inducing apoptosis, binding microtubules, and inhibiting HIF-1alpha.

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Genentech Inc. (NYSE: DNA) of South San Francisco and **Biogen Idec Inc**. (Nasdaq: BIIB) of Cambridge, Mass., said FDA has granted priority review to its supplemental biologics license application for Rituxan (Rituximab) for front-line intermediate grade or aggressive, CD20-positive, B-cell, non-Hodgkin's lymphoma in combination with cyclophosphamide, doxorubicin, vincristine and prednisone, CHOP, or other anthracycline-based chemotherapy regimens.

The sBLA filing is based on efficacy and safety data from three randomized, controlled, multicenter studies of the agent in combination with CHOP or other anthracycline-based chemotherapy induction regimens in 1,854 untreated patients with intermediate grade or aggressive, CD20-positive, B-cell, non-Hodgkin's lymphoma. All three trials evaluated the efficacy endpoint of overall survival, the company said.

Rituxan, a therapeutic antibody, targets and

selectively depletes CD20-positive B-cells without targeting stem cells or existing plasma cells, the company said.

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GlaxoSmithKline (NYSE: GSK) of Philadelphia said FDA has approved Arranon Injection (nelarabine) a chemotherapy agent, for T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma where the disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens.

The use of the agent is based on the induction of complete responses, the company said. Randomized trials demonstrating increased survival or other clinical benefit have not been conducted.

To develop Arranon for the small group of patients, GSK worked with NCI, the Children's Oncology Group and the Cancer and Leukemia Group B, in conjunction with the Southwest Oncology Group.

Arranon received accelerated approval based on complete response rates demonstrated in two phase II trials where standard treatment options had been exhausted, the company said. Post-marketing evaluation would come with a randomized, multi-center phase III trial, conducted by COG and sponsored by NCI under a Clinical Trials Agreement with GSK. The phase III study would assess both event-free survival at four years and minimal residual disease in the post-consolidation phase for standard therapy with or without nelarabine, the company said.

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ImClone Systems Inc. (Nasdaq: IMCL) of New York and **Bristol-Myers Squibb Co.** (NYSE: BMY) of Princeton, N.J., said FDA has accepted for filing the supplemental biologics license application for Erbitux, Cetuxima, for squamous cell carcinoma of the head and neck.

The application seeks approval for use in combination with radiation for locally or regionally advanced head and neck cancer, and as monotherapy for recurrent and/or metastatic disease where prior platinum-based chemotherapy has failed or where platinum-based therapy would not be appropriate, the companies said.

The Erbitux sBLA has been granted priority review, the companies said.

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Inex Pharmaceuticals Corp. (INEX; TSX: IEX) of Vancouver said a Notice of Non-Compliance from the Therapeutics Products Directorate of Health Canada.

The decision is consistent with the feedback from FDA requiring data from randomized phase III trials be generated before Marqibo could be considered for marketing approval, the company said.

Inex said it has reached agreement in principle with FDA for commercial approval for Marqibo based on phase III trial designs using complete response rate as the primary endpoint. The trials would evaluate the agent for both first-line non-Hodgkin's lymphoma and first-line acute lymphoblastic leukemia.

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NeoRx Corp. (Nasdaq: NERX) of Seattle said it has received Orphan Drug designation from FDA for its investigational product Picoplatin, a next-generation platinum therapy for small cell lung cancer.

Picoplatin is an intravenous platinum chemotherapeutic agent designed to overcome platinum resistance, the company said. In addition, testing in more than 500 patients indicates that picoplatin may have less toxicity than other platinum-based therapies.

The treatment is in an ongoing randomized, open-label, multi-center phase II trial for platinum-resistant or refractory SCLC, the company said. The trial is open to enrollment at 25 clinical sites in the U.S., with trials in Europe to begin in 2006.

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Pfizer Inc. of New York said FDA has granted the NDA priority review for Sutent, sunitinib malate, an oral, multi-targeted cancer therapy.

Pfizer said it is seeking approval for malignant gastrointestinal stromal tumor and metastatic renal cell carcinoma where tumors do not respond to standard treatment options.

Pfizer also said Sutent received similar priority review status from regulatory authorities in Canada and Switzerland. A submission for regulatory approval in the European Union was filed in August with the European Medicines Evaluation Agency, the company said.

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Viventia Biotech Inc. (TSX: VBI) of Toronto said FDA has designated Proxinium a Fast Track product for recurrent squamous cell carcinoma of the head and neck.

Proxinium combines a cytotoxic protein payload with the tumor-targeting characteristics of a monoclonal antibody, the company said. The antibody fragment of Proxinium targets EpCAM--an antigen that is expressed on many epithelial cancers including head and neck cancer, ensuring that the payload is delivered directly to the tumor. Viventia said it has been cleared by FDA and Health Canada to begin a phase II trial of the drug for chemotherapy-refractory recurrent head and neck cancer.

Clinical Trials:

Medarex To Receive Payment From BMS For Clinical Trials

(Continued from page 1)

Oligonucleotide technology, the company said.

The trial is two-phase, open-label, dose escalation study of the safety and efficacy of HYB2055 combined with a standard gemcitabine/carboplatin treatment regimen, the company said. The study would establish a primary endpoint of the phase I portion as an appropriate HYB2055 dose in combination with a fixed dose of gemcitabine/carboplatin in solid tumors, the company said. In the phase II portion, the primary endpoint is overall response rate and toxicity of the triplet combination in untreated, advanced non-small cell lung cancer. HYB2055 would be administered by subcutaneous injection once per week. Intended phase I dose levels are 4, 12, and 36 mg/week, the company said.

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Medarex Inc. (Nasdaq: MEDX) of Princeton said it expects to receive an undisclosed milestone payment from its licensing partner, **Bristol-Myers Squibb Co.**, for clinical trials of BMS-66513, a fully human antibody that targets CD137, for cancer treatment.

The antibody product was developed using the Medarex UltiMAb technology and is the first UltiMAb-derived antibody in clinical development by BMS under the December 2003 agreement with Medarex, the company said.

Medarex said it would expect additional milestone payments as well as royalties on commercial sales resulting from the development of the product.

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Millennium Pharmaceuticals Inc. (Nasdaq: MLNM) of Cambridge, Mass., said it has begun a multicenter phase I study of MLN8054, an Aurora kinase inhibitor, for advanced solid tumors.

The study would enroll 30 patients with advanced solid tumors, including lymphomas, the company said. The endpoint would determine dose-limiting toxicities and maximum tolerated dose. Secondary endpoints would include pharmacokinetics, pharmacodynamics, and preliminary assessment of anti-tumor activity. Exploratory analysis would also include the evaluation of specific molecular biomarkers.

MLN8054 is an orally administered small molecule, with specificity and potency against its target Aurora kinase, the company said. MLN8054 is administered as an oral agent, distributes widely throughout the body, and displays pharmacokinetics favorable for chronic dosing.

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Novacea Inc. of South San Francisco said it would begin a phase III AIPC Study of Calcitriol Enhancing Taxotere, or Ascent study, investigating DN-101 in combination with Taxotere versus Taxotere in combination with prednisone for prostate cancer .

The multinational 900-patient study would begin in early 2006 in Europe, the U.S. and Canada, the company said. The study chairmen would be Howard Scher, of Memorial Sloan Kettering Cancer Center; Ronald De Wit, of Erasmus University, Rotterdam, and Kim Chi, of Vancouver Cancer Centre, Vancouver.

Data from the phase II Ascent study suggested that the combination of DN-101 and Taxotere, docetaxel, reduced the occurrence of serious adverse events in advanced prostate cancer, compared to Taxotere and placebo, the company said.

An exploratory analysis of safety data from the study showed that fewer thromboembolic and gastrointestinal events were experienced with DN-101 in combination with Taxotere treatment, than treatment with Taxotere plus placebo. Serious adverse events requiring hospitalization, occurred in 27 percent receiving the combination treatment and 41 percent receiving Taxotere plus placebo, the company said.

"Based on the analyses, DN-101 in combination with Taxotere appears to improve the survival of patients receiving chemotherapy while making the treatment more tolerable and less toxic," said Tomasz Beer, director of the Prostate Cancer Program in the Oregon Health & Science University Cancer Institute. "This improved serious adverse event profile was unanticipated, and we hope to confirm these results in the phase III study of DN-101."

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Santaris Pharma of Copenhagen said the FDA has approved its IND application of a phase I/II study of SPC2996 for chronic lymphocytic leukemia.

SPC2996, part of a new class of LNA-based investigational drugs known as RNA Antagonists, reduces the level of Bcl-2 protein within tumor cells by binding and inactivating Bcl-2 messenger RNA, thereby inducing apoptosis, the company said. Bcl-2 is over-expressed in CLL cells and plays a role in pathogenesis of the disease, preventing lymphocyte apoptosis and being correlated with poor clinical outcome.

The 42-patient trial, the European arm of which is ongoing in Denmark, UK and France, is an open-label, escalating, repeated-dose, multi-center study of

SPC2996 for relapsed or refractory CLL, the company said. The primary objective is safety and efficacy.

The first U.S. center to join the study would be the Holden Comprehensive Cancer Center at the University of Iowa under the direction of James Wooldridge.

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Spectrum Pharmaceuticals Inc. (Nasdaq: SPPI) of Irvine, Calif., said its development partner, **GPC Biotech AG** (Frankfurt Stock Exchange: GPC; Nasdaq: GPCB) has begun a phase II study evaluating saraplatin for metastatic breast cancer where no more than one chemotherapy treatment regimen has occurred.

The open label, multicenter study, which is managed by US Oncology, is being conducted at fifty-seven research sites in the US Oncology Network, the company said. The primary objective is to determine the objective response rate of satraplatin in 80 patients.

The oral investigational drug, is a member of the platinum family of compounds, the company said. Satraplatin is in a phase III registration trial as a second-line chemotherapy treatment for hormone- refractory prostate cancer, the company said.

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Sunesis Pharmaceuticals Inc. (Nasdaq: SNSS) of South San Francisco said it has begun a phase I trial of SNS-595, an anti-cancer small molecule drug for refractory acute leukemias.

SNS-595 is a cell cycle modulator that induces apoptosis, the company said.

The open-label, multi-center, dose-escalation study would examine the safety, tolerability and pharmacokinetics of the agent SNS-595 to establish an optimal dosing regimen for phase II testing of patients in relapsed or refractory acute myelocytic leukemia and other acute leukemias, the company said.

Enrollment for acute refractory leukemias will be at three centers in the U.S., including the H. Lee Moffitt Cancer Center & Research Institute, MD Anderson Cancer Center and the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University, the company said.

Deals & Collaborations:

American BioScience Licenses Abraxane To Taiho In Japan

American BioScience Inc. of Santa Monica, Calif., said it has licensed Abraxane to **Taiho Pharmaceutical Co. Ltd.** of Tokyo and has established a Joint Steering Committee with Taiho to oversee development in Japan for breast, lung, gastric, and other solid tumors.

Abraxis Oncology, a division of American Pharmaceutical Partners Inc. (Nasdaq: APPX), is commercializing Abraxane in North America, the company said.

Under the agreement, ABI said it would receive upfront and milestone payments in excess of $50 million, in addition to royalties. ABI would supply Abraxane for the Japanese market.

Abraxane for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) was approved by FDA in January 2005, the company said. It is indicated for breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy. ABI said a development program is underway to expand the indications in breast, lung, ovarian, head and neck, and melanoma cancers.

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AVEO Pharmaceuticals Inc. of Cambridge, Mass., said it has signed a second oncology-focused collaborative agreement with **Merck & Co. Inc**.

Under the agreement, Merck and AVEO said they have established a two-year alliance to conduct preclinical studies on cancer compounds using the AVEO Human Response Prediction platform. Merck has exclusive rights to the data generated from the studies that relate to its proprietary compounds. Financial terms include an equity investment by Merck in AVEO, annual research funding for AVEO and the potential for milestone payments to AVEO, the company said.

The HRP platform is based on the AVEO proprietary, genetically-defined mouse models of human cancer, the company said. Each of the models contains signature genetic mutations that are present in human disease.

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BioWa Inc. of Princeton and **OncoTherapy Science Inc.** of Kawasaki, Japan, said they have entered into a collaboration to identify and develop anti-cancer monoclonal antibodies.

OncoTherapy Science would employ its technology for identification of the cancer antigens and generation of Mabs against those antigens, and BioWa would apply its Potelligent technology to the Mabs to enhance antibody-dependent cellular cytotoxicity, the companies said.

The collaboration would create antibody therapeutics with improved biological properties targeting membrane antigens, the companies said. Under the partnership, BioWa and OncoTherapy Science would share profits gained from future antibody products, the companies said.

The technology reduces the amount of fuctose in the carbohydrate structure of an antibody using a proprietary fucosyltransferase-knockout host cell line as a production cell, the companies said. Data demonstrate that Potelligent technology increases the potency and efficacy of such antibody in vivo.

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ChemDiv Inc. of San Diego and **ProQinase GmbH** of Freiburg, Germany, said they have established a partnership in the discovery and preclinical development of kinase inhibitors.

ChemDiv said it would support design and synthesis of target-focused small molecule libraries, undertake medicinal chemistry for hit to lead and lead optimization, as well as DMPK and certain in vivo experiments. ProQinase said it would be responsible for in vitro kinase inhibitor screening and profiling on a panel of jointly selected oncology-relevant kinase targets, cellular assays and in vivo experiments. Both parties would share development costs and revenues from the planned out-licensing of optimized leads.

ProQinase GmbH is a division of the KTB Tumorforschungs GmbH at the Tumor Biology Center Freiburg, Germany.

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ChondroGene Ltd. (TSX Venture: CDG) of Toronto said it has entered into an agreement with the Division of Research of the **Permanente Medical Group** of Northern California, to develop a research database infrastructure for genomic research.

The genomic database would serve as a repository of clinical information generated by Kaiser Permanente researchers for assays that use the ChondroGene proprietary Sentinel Principle. The objectives of the database when implemented are to standardize and achieve consistency in the format of data for future studies. The common format would also facilitate testing of biospecimens at ChondroGene, as agreed upon by the Kaiser Permanente Division of Research and ChondroGene, the company said.

The Sentinel Principle detects and stages diseases or medical conditions from a blood sample, the company said.

The Permanente Medical Group of Northern California is one of eight multi-specialty physician groups that are part of Kaiser Permanente, an integrated health care organization with over 8.3 million members in nine states, the company said.

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DiagnoCure Inc. (TSX: CUR) of Quebec City said it has signed a licensing agreement with **Genzyme Corp**. (Nasdaq: GENZ) for worldwide exclusive rights to lung cancer associated genes.

DiagnoCure said it would pay upfront and milestone payments as well as royalties on sales of products. In exchange, Diagnocure would gain access to Genzyme intellectual property covering gene sequences related to the detection of lung cancer. Also under the agreement, DiagnoCure has granted to Genzyme an option to become its commercialization partner for any diagnostic product developed using one or more of the licensed genes, the company said.

In 2004, data from an early study with a prototype lung cancer assay using bronchial aspirates as a sample were promising, the company said. The test detected over 90 percent of the cancers against 37 percent with routine cytology.

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Morphotek Inc. of Exton, Penn., said it has entered into a collaboration with the **John Wayne Cancer Institute** for the discovery and development of therapeutic antibodies for melanoma and lung cancer.

Morphotek said it would apply its proprietary Human Morphodoma antibody technology to advanced melanoma, lung cancer and other solid malignancies that express the antigen. Donald Morton, medical director and surgeon-in-chief would lead the JWCI initiative in characterizing and evaluating the specificity and efficacy of the antibodies in bench studies and clinical trials, the company said.

Human Morphodoma is an antibody development platform that employs morphogenics to yield fully human, monoclonal antibodies from high-titer hybridoma cells, the company said.

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Par Pharmaceutical Companies Inc. (NYSE: PRX) of Spring Valley, N.Y., said it has entered into an agreement with **Valeant Pharmaceuticals North America** to promote the antiemetic drug Cesamet, nabilone, capsules following approval by FDA for chemotherapy-induced emesis.

Par would promote Cesamet to physicians in the U.S., and Valeant would record sales of the product and fund marketing associated expenses, the company said.

Valeant said it acquired Cesamet from Eli Lilly & Co. in 2004 and markets the product in Canada. Cesamet holds 85 percent share of total prescriptions in the Canadian cannabinoid market, the company said.

Cesamet, cannabinoid treatment, would be marketed for nausea and vomiting associated with cancer chemotherapy when there is no response to

conventional antiemetic treatments, the company said.

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Peregrine Pharmaceuticals Inc. (Nasdaq: PPHM) of Tustin, Calif., said the U.S. Department of Defense Prostate Cancer Research Program has awarded a grant totaling $582,988 to the University of Texas Southwestern Medical Center at Dallas to study vascular targeting antibodies in combination with chemotherapy for prostate cancer treatment.

Philip Thorpe, professor of pharmacology at the University of Texas Southwestern Medical Center, member of the Peregrine Scientific Resource Board and an inventor of the technology, is principal investigator, the company said.

Tarvacin Anti-Cancer, the Peregrine vascular targeting antibody, which is in a phase I trial for advanced refractory solid tumors, would be studied to assess its use in combination with other cancer agents, the company said.

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Schering AG (NYSE: SHR ; FDE: SCH) of Berlin and **Sonus Pharmaceuticals Inc.** (Nasdaq: SNUS) of Seattle said they have signed an agreement granting Schering an exclusive, worldwide license to the **Sonus** Tocosol Paclitaxel anti-cancer product.

Under the agreement Schering would take 15 percent equity investment in Sonus., which also would receive an upfront fee, milestone payments and royalties, the companies said.

Tocosol Paclitaxel is a vitamin E-based emulsion formulation that allows a dose of paclitaxel to be delivered in a 15-minute infusion, the companies said. The formulation delivers 70 percent more active paclitaxel compared to an equal dose of Taxol. It is cremaphor-free, which allows for shorter infusion times and improves tolerability, the companies said.

The product has shown promising safety and anti-tumor activity in phase II trials in a variety of solid tumors, and is in a phase III study for metastatic breast cancer, the companies said.

An ongoing phase II study of Tocosol Paclitaxel in metastatic breast cancer has shown a confirmed objective response rate of 53 percent in 47 patients, the companies said. Additional phase II studies of the formulation demonstrated objective response rates of 21 percent in 42 patients with non-small cell lung cancer, 33 percent in 27 with bladder cancer and 39 percent in 51 with ovarian cancer.

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Schering-Plough Corp. (NYSE: SGP) and **Oncomethylome Sciences** said they have entered into a collaboration and license agreement in which Schering-Plough would use assay technology from OS that measures the methylation status of the MGMT gene for glioblastoma multiforme, which is being treated with temodar, temozolomide.

The DNA methylation status of the MGMT gene is being evaluated for role in Temodar therapy for GBM brain cancer, the companies said.

Oncomethylome Sciences would receive an upfront license payment, milestone payments and sample processing fees from Schering-Plough, the companies said.

The assay was developed Johns Hopkins University researchers in 2000, the companies said.

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Stem Cell Sciences plc (AIM: STEM) of Edinburgh, Scotland, said it has granted to **Lexicon Genetics Inc**. (Nasdaq: LEXG) of The Woodlands, Tex., an exclusive license to its proprietary Internal Ribosome Entry Site technology for genetically modified mice.

The technology is used to enhance the accuracy of gene expression in genetically altered mice and cultured stem cells, the company said.

SCS said it would grant the license subject to non-exclusive licenses previously granted by SCS, which extends through the life of the IRES technology patents and provides Lexicon with the right to grant sub- licenses in the U.S. and Europe.

Lexicon would provide SCS with an upfront payment and share with SCS future revenues generated by sublicenses to the IRES technology, the company said. Lexicon has granted SCS certain non- exclusive rights under patents controlled by Lexicon covering its proprietary gene targeting technology for use in stem cell and progenitor cell lines.

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Third Wave Technologies Inc. (Nasdaq: TWTI) of Madison, Wisc., said it has formed a preferred marketing relationship with **Genzyme Genetics** to provide testing in North America with the Invader UGT1A1 Molecular Assay for colorectal cancer when the treatment is Camptosar, irinotecan.

The assay identifies increased risk for adverse reactions to Camptosar by detecting variations in the UGT1A1 gene associated with that risk, the company said. Data from a clinical study indicate that in the population at increased risk, one of the variations have a greater than nine-fold increased possibility of experiencing toxicity from Camptosar than without it. Camptosar labeling was recently updated to include dosing recommendations based on UGT1A1 status.