THE CANCER LETTER INTERACTIVE

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NCAB Puts 20% Cap On P01 Budget Raises To Stem Requests Exceeding NCI's Funds

NCI advisors last week approved a cap on the amount that investigators with program project (P01) grants can request when they apply for competing continuation of their awards.

The National Cancer Advisory Board unanimously approved the imposition of a 20 percent cap on "type 2" P01 grant application budget requests at its meeting Feb. 16. NCI immediately put the policy in place.

The policy was necessary because P01 investigators have been requesting budget increases of 40 to 50 percent, far above NCI's 14 percent budget increase, and twice the 20 percent increase in NCI funding

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In Brief:

Bishop Completes Term As NCAB Chairman; Terms Of Five Extended Awaiting W.H. Action

J. MICHAEL BISHOP completed his term as chairman of the National Cancer Advisory Board at the board's Feb. 16 meeting. "It has been a great privilege to work with the board," Bishop said. "I'd like to acknowledge the superb work of the National Cancer Institute, its staff, [NCI Director **Richard Klausner**], and immediate colleagues. This is federal government at its best." Bishop recently received the Knudson Award, given by the NCI Intramural Program at the program's retreat. The terms of five other NCAB members were scheduled to expire in March, but NCI requested 180-day extensions so they can attend the board's June meeting if the White House hasn't appointed their successors by then. Bishop said his duties at University of California, San Francisco, prevent his further service on the board. The five who will complete their terms—eventually—this year are: **Kay Dickersin**, Brown University; **Alfred Goldson**, of Howard University; **Arthur Nienhuis**, director, St. Jude Children's Research Hospital; **Philip Schein**, University of Pennsylvania; and **Vainutis Vaitkevicius**, president emeritus, Karmanos Cancer Institute. . . . **UNIVERSITY OF CALIFORNIA AT IRVINE** School of Medicine received a $8.1 million gift to expand research and education on cancer genetics which will include a study on cancers specific to Asian Americans. The gift was presented by the Chao family to create a cancer genetics program geared to Asian Americans. **Ken Chang**, UCI associate professor of medicine, was appointed director of the H.H. Chao Memorial Intervention Endoscopy Suite. The gift also will be used to establish a community education program, conduct clinical trials, set

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P01 Grantees Seek Increases Of 40-50%; NCI Can't Pay

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for P01s this fiscal year, said Marvin Kalt, director of the Division of Extramural Activities. Almost half of NCI funding for P01s in any fiscal year goes to type 2 continuation awards, he said.

"It is preferable to review applications designed to fit realistically within budgets, rather than to continue to allow unlimited budget requests, only to make steep administrative cuts prior to an award, since such changes may substantially alter the scope, and therefore, potentially the merit of a proposed P01," according to a document Kalt submitted to the NCAB.

P01 investigators still would be eligible to receive supplemental awards that NCI provides for specific purposes, Kalt said. NCI estimates receiving 48 type 2 requests this year, and projects a success rate for these grants of 54.2 percent.

NCI also provides supplemental funding for "special requests because of unusual needs," NCI Director Richard Klausner said.

"The major reason for [the cap] is to try to get some greater sense of predictability about what is going to happen to the budget," Klausner said. "In watching what's happened, we felt this was a reasonable experiment giving us enough flexibility and ability to look at individual cases that we felt we would not be hurting the science."

Overall, grant application funding requests are increasing faster than NCI anticipated in the second and third funding rounds for fiscal year 2000, Klausner said. Third-round funding increase requests for R01 grants are up 10 percent, he said.

NCI may have a $20 million shortfall of funding for research project grants, Klausner said.

"We will have to work on finding this [money] in the Director's reserve, which is shrinking rapidly, and from a variety of funding approaches," Klausner said.

No Lack Of Enthusiasm For P01s

The new policy for P01s doesn't appear to signal a lack of enthusiasm for the grant mechanism within NCI. When NCAB member Frederick Li, of Dana-Farber Cancer Institute, asked whether NCI had "made an assessment of 'bang for buck' of P01s versus R01s," Klausner spoke at length about the inability to make an accurate comparison.

"One can readily write down some potential measures, like publications," Klausner began. "Very quickly, you get into how do you value one publication versus another? You might do that by citation index. That would take time.

"We have these conversations quite a lot about 'bang for the buck,' or how do we evaluate in some quantitative way the different [funding] mechanisms," Klausner said. "One also has to ask whether the different mechanisms allow types of science or questions to be asked or addressed that other types of funding mechanisms don't.

"One could put R01s and P01s on the same playing field and say, 'Let's look at publications,' but if there is research that would only get out [through] the collaboration that a P01 gives you, then it's not clear that without somehow addressing that, a formalism of output would give you the answer you're looking for," Klausner said. "We've talked about this around and around … and did not come up with a satisfactory way to agree upon 'bang for the buck' measurements."

Li said P01s tend to be awarded to large centers or institutions that already have many grants.

"Fred, I wonder whether you can make some of the opposite conclusions," Klausner replied. "There are places that don't have the breadth to become, for example, a cancer center, but in some specific areas have special expertise with a critical mass, and have been extremely successful…. There are some

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very good examples of that, where they actually level the playing field. I think there is something valuable about the fact that we have a mix.

"There is a change of people moving toward collaborative, interactive grants, and recognizing the need for enhanced funding mechanisms for repositories, registries, informatics, technology," Klausner said. "I think that represents a real movement in science. I suspect P01 line is going to be more and more stressed."

NCI's plans to expand funding for Specialized Programs of Research Excellence over the next five years in all cancers and to create alternative SPORE grants for research in cellular pathways and mechanisms, also may create greater demand for P01 grants, Klausner said.

"The community seems to want to use these sorts of collaborative, interactive mechanisms, and perhaps, in some way, that is a measure of the value of the mechanisms," Klausner said.

Following is the text of the new policy:

To align more closely budgetary increases for P01 program project awards with overall NCI budget growth, beginning with the June 1, 2000 receipt date, budget requests for direct costs for NCI supported competing continuation (type 2) Program Project (P01) Grants must not exceed an increase of 20% over the direct costs awarded in the last non-competing (Type 5) year. Subsequent future year budget requests of competing continuations cannot, over the life of the proposed project, exceed simple inflationary adjustments. This dollar total is exclusive of sub-contractual indirect costs that appear as a direct cost in the budget of the applicant organization.

Where currently active supplements have been awarded in conjunction with ongoing programs, the supplemental direct cost may be added into the base of the parent award if the work done under the supplement is to continue in the new project period. Regardless of peer reviewed recommended budgets, all awards still will be subject to any future overall NIH and NCI cost containment principles in effect at the time of an award. After a competing award has been issued, awardees will continue to be eligible to apply for all competing and administrative program project supplements, even if the additional supplemental request exceeds the original cap.

It is recognized that in some epidemiological or clinical research programs, the last non-competing year budget may be substantially lower than other previous years. In such circumstances, if the nature of the new research requires budget increases for one or more interim years above the 20 percent rule for the last non-competing year, applicants may cite the most relevant prior budget year as a base for the new cap. Such applicants are advised to contact the NCI program director for the currently funded grant for advice before submitting an application. Prior approval of the NCI will be required before any application with a budget exceeding these guidelines can be accepted for receipt and review.

Competing continuation applications requesting increases in excess of these guidelines lacking such approval will be returned without review.

NCI P01 grant policies and procedures are available at http://deainfo.nci.nih.gov/awards/P01.htm.

Drug Development:

NCI, SAIC To Support Contracts For Molecular Target Labs

Taking the next major step in its effort to form a national infrastructure for the development of therapies targeted to molecular changes in cancer cells, NCI plans to support laboratory research that would identify specific ligands for key components of critical biological pathways.

The contracts would fund "Molecular Target Laboratories" that would identify ligands that may be used as chemical probes for biological processes, probes that can be imaged for physiological and biochemical monitoring, and as potential candidates for clinical trials, according to a pre-solicitation notice.

The MTLs would derive drug candidates, imaging probes, and perturbational probes. In time, the MTLs may also acquire or redirect their capacity to enable translation of drug candidates and imaging probes from the laboratory to the clinic, and may eventually contain fully developed programs in ligand discovery, drug and probe development, and possibly clinical testing, according to the notice.

Conference March 14 For Applicants

Science Applications International Corp., the operations and technical support contractor at the NCI Frederick Cancer Research and Development Center, would issue the contracts.

SAIC plans to fund "multiple" contracts, and the amount of funding for the program is flexible, an SAIC spokesman said.

NCI and SAIC want to get a better idea of the capabilities of applicants before discussing the amount of funding, the spokesman said.

To do that, SAIC has scheduled a pre-solicitation conference for March 14, for investigators interested in applying for the contracts.

The conference will be held at the Holiday Inn, in Bethesda, MD, from 10 a.m. to 1 p.m. Further information and a registration form are available at http://www.ncifcrf.gov/mtl.

A draft solicitation is available by contacting Heather Wells, phone 301-846-1520 or fax to 301-846-5414.

According to the pre-solicitation notice, the multi-year program will have an initial one-year contract with multiple option years. Each MTL would be expected to have: capability to allow design and implementation of biological, synthetic, or biochemical screens; chemistry for library synthesis; practice of high-throughput screening; resynthesis; radiochemical and imaging expertise; biological testing (at least at the in vitro level); demonstrated capacity to include molecules for cancer treatment and imaging or diagnostics as successful outcomes of their research programs; an independent business management system to support MTL activities.

The ultimate products of the MTLs will be repositories of chemicals, assays, and information, including:

—Cancer-relevant target assays, suitable for high-throughput screening of chemical libraries. These assays will not be claimed as intellectual property and will be made publicly available.

—Chemical libraries: these will constitute the principal sources of chemical diversity to be interrogated by the biological assays developed in the MTLs. This collection of libraries will constitute an invaluable public resource and will therefore be made available by the MTLs to qualified research groups in a manner to be established by the MTLs and NCI.

—Chemical probes for biological studies. Ligands with important biochemical or phenotypic effects will be placed into a repository and made available to qualified research groups.

—Information: the identification of biologically active small molecules and the relation of particular chemical structures to biochemical activity and cellular phenotype. This information will be maximally useful to the research community to the extent that it is made publicly available expeditiously and systematically. To accomplish this goal, the MTLs will work with SAIC and NCI to construct a publicly available database relating chemical structure to biological function. This database will be populated with data from research projects in the MTLs as soon as possible after discovery, verification and IP review. This database will also incorporate data from other qualified research groups in the cancer research community wishing to contribute to it. NCI envisages that it will, in time, serve a role for ligand discovery efforts analogous to that of DNA sequence databases for gene discovery.

According to the pre-solicitation notice, NCI hopes to make the new technologies developed by MTLs under these contracts available, as much as possible, to the research community. For the MTLs, NCI will invoke the provision of the Bayh-Dole Act that enables the government to restrict or eliminate the right to retain title "in exceptional circumstances when it is determined by the agency that restriction or elimination of the [contractor/subcontractor's] right to retain title to any subject invention will better promote the policy and objectives of [the Bayh-Dole Act]."

Thus, the "Determination of Exceptional Circumstances" will enable NCI to either elect title to inventions developed by the MTLs under these contracts, or to grant greater rights to such inventions to the MTL.

NCAB News:

An Extraordinary Opportunity For Budgetary Coordination

Public officials are often accused of saying one thing while doing exactly the opposite.

So a Presidential appointee who can demonstrate the coordination of plans and outcome will have an easier time dealing with members of Congress.

But when NCI Director Richard Klausner wore a tie that was remarkably similar in pattern to a budget chart the Institute sent to a Congressional committee last week, he might have set a new standard in legislative relations.

Klausner enjoys a reputation in Washington as a leader in government "reinvention," but has not been known as one of the city's fashion trend-setters. Except for occasional gigs with his rock 'n' roll band, for which he wears black, Klausner usually sports the classic uniform of male NIH scientists: charcoal or gray slacks; white or cream shirt; jacket and tie

for important events; and comfortable, well-worn shoes.

Thus, it might have been mere coincidence that on Feb. 15, appearing before the House Labor, HHS, Education Appropriations Subcommittee, Klausner wore a copper-circle patterned tie that was remarkably similar to the pattern selected for the "Extraordinary Opportunities 29.7%" section of one of four pie charts submitted to the committee.

The colorful pie charts—in solids, stripes, plaids, and circles of blue, brown, purple, yellow, and red—illustrate how NCI is spending its $420 million budget increase. NCI staff prepared the charts because word had come down that the subcommittee would be interested in the stewardship of the Institute's share of last year's $2 billion increase for NIH.

However, Klausner did not mention the pie charts in his testimony. Using line graphs propped on an easel, he discussed the downward trend in cancer mortality (**The Cancer Letter**, Feb. 18).

Had Klausner referred to the budget charts, members of Congress probably wouldn't have noticed the striking resemblance between pie and tie. Most were too busy squinting through magnifying glasses at the NCI Lymphochips placed at their seats.

The day after the hearing, unconstrained by jacket or tie, Klausner had the opportunity to wax enthusiastic about the pie charts.

NCI is spending 84 percent of its $420 million increase on the priorities outlined in the Institute's professional judgment budget, Klausner said to the National Cancer Advisory Board at it Feb. 16 meeting.

"We have only achieved this level of alignment with our planning process with the fiscal year 2000 budget distribution," Klausner said. "I am very pleased about this."

Besides allocating 29.7 percent of the increase for "Extraordinary Opportunities"—the copper-circle slice—NCI will spend 53.5 percent on initiatives in the "Challenge" section (blue-and-white stripe) of the FY2000 Bypass budget. The remaining 16.8 percent of the increase (pale yellow) is going to other areas.

Almost 30 percent of the increase will fund investigator-initiated research, according to a blue, brown, and purple pie chart.

"This is one more step in the process of engaging the research community… in knowing upfront what our priorities are and how they link to programs and initiatives, and demonstrating that, not only to them, but [also] to Congress," Klausner said in presenting the charts to the NCAB.

The board met in a teleconference.

Anticipating that no matter how programmatically or esthetically pleasing the charts were, NCAB members phoning in to the meeting wouldn't haven been able to see them, NCI staff sent "embargoed" packets to the board several days earlier.

Nevertheless, a question remained: Did the charts influence Klausner's wardrobe planning for the hearing?

NCI Legislative Liaison Dorothy Foellmer, who wore a dark purple outfit that perfectly matched one section of a pie chart, declined to comment. She referred questions to Klausner.

Confronted after the teleconference, Klausner replied, "Now you know."

NCAB Comments On Patient Privacy

NCAB voted unanimously to send comments to HHS Secretary Donna Shalala expressing concern about a proposed rule designed to protect the privacy of patient medical records stored electronically.

The board said provisions of the proposed rule would serve to impede research. In particular, a requirement for patients to sign two separate authorizations in addition to an informed consent statement would be a "substantive impediment," the board said.

The NCAB letter will be one of about 40,000 the department has received commenting on the proposed rule. The deparment is likely to take several months to review the comments, sources said.

The HHS proposed rule is available at http://aspe.hhs.gov/adminsimp/.

NCAB Forms Two Subcommittees

NCAB voted unanimously to form two new subcommittees: the Ad Hoc Subcommittee on Communications and the Ad Hoc Subcommittee on Confidentiality of Patient Data.

Susan Love, adjunct professor, University of California School of Medicine, will serve as chairman of the communications subcommittee. Susan Sieber, acting director of the NCI Office of Communications, will serve as executive secretary.

Co-chairmen of the confidentiality subcommittee are Kay Dickersin, associate professor, Brown University, in her role as a member of the National Breast Cancer Coalition, and Frederick Li, chief of cancer epidemiology and control, Dana-Farber Cancer Institute. Mary McCabe, director of the NCI

Office of Clinical Research Promotion, will serve as executive secretary.

Board To Commend Porter

NCAB plans to draft a resolution to commend Rep. John Porter (R-IL) on his service as chairman of the House Labor, HHS, Education Appropriations Subcommittee.

Funding Opportunities:

RFAs Available

RFA CA-00-002: Molecular Target Drug Discovery for Cancer

Letter of Intent Receipt Date: June 6, 2000

Application Receipt Date: July 18, 2000

NCI's Developmental Therapeutics Program and the NCI Chemoprevention Agent Development Research Group invite cooperative agreement applications to exploit molecular targets for drug discovery.

NCI is reorganizing its drug development programs from early drug discovery phases to the conduct of clinical trials in order to bring forward new types of agents based on strong rationales. The plan also involves changes in the clinical evaluation of new agents that will include appropriate measurements to verify target modulation.

Projects are acceptable at all stages of development, including mature projects as well as novel insights at an early investigational stage. However, the cooperative agreements should be projects that are more developed and comprehensive.

NCI has budgeted $3 million total costs for the first year of funding and expects to make 8-10 awards for periods up to four years.

Inquiries: Toby Friedberg, Referral Officer, Division of Extramural Activities, 6116 Executive Blvd., Room 8062, MSC 8239, NCI, Bethesda MD 20892-8239, Rockville, MD 20852 (express courier), phone 301-496-3428; fax 301-402-0275; e-mail: tf12w@nih.gov

RFA HD-00-004: Mutagenesis Screens/ Phenotyping Tools for Zebrafish

Letter of Intent Receipt Date: April 16, 2000

Application Receipt Date: May 19, 2000

The RFA is the result of an NIH initiative with participating Institutes working though the Trans-NIH Zebrafish Coordinating Committee under the co-chairmanship of the National Institute of Child Health and Human Development and the National Institute of Diabetes and Digestive and Kidney Diseases.

The RFA, which will use the NIH R01 award mechanism, encourages research designed to exploit the power of mutagenesis screening in zebrafish in order to detect and characterize genes, pathways, and phenotypes of interest in development, behavior, organ formation, disease processes and aging. Applications that propose to advance the technologies associated with such phenotyping also are welcome.

The participating ICs intend to commit approximately $4.5 million in total costs in FY 2001 to fund 8 to 10 new grants in response to this RFA. An applicant may request a project period of up to five years and a budget for direct costs of up to $250,000 per year.

Inquiries: http://www.nichd.nih.gov/rfa/hd-00-004/hd-00-004.htm.

RFA: The NCI Scholars Program

The purpose of this reissued RFA is to continue to provide an opportunity for new investigators with outstanding abilities and research experience in the basic, clinical or population-based (e.g., epidemiological, behavioral, prevention or control) sciences, mathematics, or in technology-based research, obtained in a variety of environments (e.g., academic, industry, government) and with no more than five years of postdoctoral research training experience (clinical training does not count against the five years of research experience), to establish their first independent cancer research program within the special environment of the NCI and to continue their careers at an institution of their choice.

The NCI Scholars Program provides the necessary resources to initiate an independent research program for three to four years in the NCI Intramural laboratories, followed by support through an extramural funding mechanism (K22) of their research program for two years at the extramural institution to which they are recruited.

Inquiries:LesterGorelic, Program Director, Office of Deputy Director of Extramural Sciences, Cancer Training Branch, phone: 301-496-8580, e-mail: lg2h@nih.gov

Change of Receipt Date for Interdisciplinary Research Teams for Molecular Target Assessment

NCI gives notice of a change of receipt date for applications submitted in response to RFA CA-00-001, Interdisciplinary Research Teams For Molecular Target Assessment.

The RFA can be accessed at: http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-00-001.html.

The previous receipt date of March 15, 2000 has been changed to June 20, 2000.

The new application receipt date of June 20, 2000, results in the following revised schedule:

Letter of Intent Receipt Date: April 14, 2000

Application Receipt Date: June 20, 2000

NCAB Meeting Date: Feb. 12-14, 2001

Earliest Award Date: April 1, 2001

Inquiries: Louise Grochow, chief, Investigational Drug Branch, CTEP, DCTD, NCI, Executive Plaza North, Room 715, 6130 Executive Blvd, Rockville, MD 20850, phone 301-496-1196; fax 301-402 0428; e-mail grochowl@ctep.nci.nih.gov

Program Announcements

PAR-00-060: Molecular Target Drug Discovery for Cancer: Exploratory Grants

Letter of Intent Receipt Date: June 6, 2000

Application Receipt Date: July 18, 2000

Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, NCI, and the Chemoprevention Agent Development Research Group, Division of Cancer Prevention, NCI, invite exploratory/ developmental grant applications R21 to exploit molecular targets for drug discovery.

Inquiries: Toby Friedberg, Referral Officer, Division of Extramural Activities, NCI, 6116 Executive Blvd., Rm 8062, MSC 8239, Bethesda, MD 20892-8239, Rockville, MD 20852 (for express/courier service), phone 301-496-3428; fax 301-402-0275; e-mail: tf12w@nih.gov

PAR-00-061: Molecular Target Drug Discovery for Cancer: Small Business Grants

Letter of Intent Receipt Date: June 6, 2000

Application Receipt Date: July 18, 2000

Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, NCI, and the Chemoprevention Agent Development Research Group, the Division of Cancer Prevention, NCI invite Small Business Innovative Research Programs Small Business Technology Transfer Program applications to exploit molecular targets for drug discovery. Support for the PA is through the SBIR and STTR mechanisms.

Inquiries: Toby Friedberg, Referral Officer, Division of Extramural Activities, NCI, 6116 Executive Blvd., Rm 8062, MSC 8239, Bethesda, MD 20892-8239, Rockville, MD 20852 (for express/courier service), phone 301-496-3428; fax 301-402-0275; e-mail tf12w@nih.gov

PAR-00-062: Molecular Target Drug Discovery for Cancer: Competing Supplements

Letter of Intent Receipt Date: June 6, 2000

Application Receipt Date: July 18, 2000

Developmental Therapeutics Program, Division of Cancer Treatment and Diagnosis, NCI, and the Chemoprevention Agent Development Research Group, Division of Cancer Prevention, NCI invite competitive supplement applications for existing NIH grants to exploit molecular targets for drug discovery.

Inquiries: Toby Friedberg, Referral Officer, Division of Extramural Activities, NCI, 6116 Executive Blvd., Rm 8062, MSC 8239, Bethesda, MD 20892-8239, Rockville, MD 20852 (for express/courier service), phone 301-496-3428; fax 301-402-0275; e-mail: tf12w@nih.gov

PAR-00-063: Institutional Clinical Oncology Research Career Development Program

Letter of Intent Receipt Date: May 1 annually

Application Receipt Date: June 1 annually

The purpose of the NCI program is to increase the number of medical doctors and doctorally degreed Oncology Registered Nurses who are motivated and properly trained to: (1) communicate and collaborate with basic/behavioral research scientists in order to expedite the translation of basic/ behavioral research information into patient-oriented cancer research; (2) perform independent clinical oncology research that develops and tests rational scientific hypotheses based on fundamental and clinical research findings with the potential for improving the medical care of cancer patients; and (3) design and test innovative clinical protocols and manage all phases of clinical trials research.

To achieve this purpose, awards are made to institutions for up to five years for the development and implementation of training programs providing clinicians with all of the necessary information and training that will enable them to design, implement and manage all phases of cancer clinical trials research.

Patient-oriented research is defined as research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator directly interacts with human subjects. These areas of research include: 1) mechanisms of human disease; 2) therapeutic interventions; 3) clinical trials; and 4) the development of new technologies.

Support of this program will be through the NIH Mentored Clinical Scientist Development Program award or K12 mechanism.

Inquiries: Lester Gorelic, Cancer Training Branch, Office of Centers, Training and Resources, NCI, 6116 Executive Blvd., Suite 7011, MSC 8346, Bethesda, MD 20892-8346, phone 301-496-8580; fax 301-402-4472, e-mail: lg2h@nih.gov

PAR-00-064: Cancer Education and Career Development Program

The purpose of this specialized Cancer Education Program is for the development and implementation of curriculum-dependent programs to train predoctoral and postdoctoral candidates in cancer research settings that are highly inter-disciplinary and collaborative. The program is applicable to cancer prevention and control, epidemiology, nutrition, and the behavioral and population sciences; but should also be considered by other highly interdisciplinary areas of research such as imaging and molecular diagnosis that will require sustained leadership, dedicated faculty time, specialized curriculum development and implementation, interdisciplinary research environments, and more than one mentor per program participant to achieve their education and research career development objectives. The PA will use the R25 grant.

Inquiries: Lisa Begg, Cancer Training Branch, Office of Centers, Training and Resources, NCI, 6116 Executive Blvd, Suite 7011, MSC 8346, Bethesda, MD 20892-8346, fax 301-402-4472; e-mail beggl@mail.nih.gov

PAR-00-066: The Howard Temin Award

The goal of the NCI Howard Temin Award is to bridge the transition from a mentored research environment to an independent research career for scientists who have demonstrated unusually high potential during their initial stages of training and development. This special award is aimed at fostering the research careers of outstanding junior scientists in basic research who are committed to developing research programs directly relevant to the understanding of human biology and human disease as it relates to the etiology, pathogenesis, prevention, diagnosis, and treatment of human cancer. The major objective of the award is to sustain and advance the early research careers of the most promising M.D.s and Ph.D.s while they consolidate and focus their independent research programs, and obtain their own research grant support. The Temin Award offers up to five years to develop knowledge in basic sciences and research skills, with up to three of the initial years (at least one year required) in a mentored environment followed by a transition to an unmentored phase.

The candidate must have a research or a health professional doctorate or its equivalent, must have completed at least three years of postdoctoral research at the time of award, and must have demonstrated highly productive research activity and the potential for establishing an independent research program in the period after the doctorate. Recipients of an NCI Preventive Oncology/Population Sciences Career Development (K07) Award, a Mentored Clinical Research Scientist Career Development (K08) Award or a Mentored Patient-Oriented Research Career Development (K23) Award in their last two years of support are also eligible to apply.

Inquiries: Andrew Vargosko, Office of Centers, Training and Resources, NCI, 6116 Executive Blvd., Suite 7011 MSC/8346 Bethesda, MD 20892-8346, phone 301- 496-8580, fax: 301-402-4472, email: av8b@nih.gov.

In Brief:

UNC Lineberger Appoints Two; Zaret Wins Chair At Fox Chase

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up a gene array system and to complete construction on the Chao Family Cancer and Genetics Laboratories, said Frank Leyskens, director of the Chao Family Comprehensive Cancer Center. . . . **MARCI CAMPBELL** and **ANDREW OLSHAN** were appointed program leaders at the University of North Carolina Lineberger Comprehensive Cancer Center. Campbell, assistant professor of nutrition at UNC School of Public Health, will lead the Cancer Prevention and Control Program. Olshan, associate professor of epidemiology at UNC School of Public Health and research associate professor in the Department of Surgery, School of Medicine, will lead the Cancer Epidemiology Program . . . . **KENNETH ZARET,** head of the scientific program in cell and developmental biology at Fox Chase Cancer Center, was appointed the first William Wikoff Smith Chair in Cancer Research. The $1.5 million endowment for the faculty chair was given by the W.W. Smith Charitable Trust of Newtown, PA, as part of the $38 million campaign to fund the Research Institute for Cancer Prevention and will help support Zaret's endoderm cell research by funding laboratory personnel, equipment and supplies. . . . **FOX CHASE** radiation oncology department will open the first MRI for cancer radiation treatment planning on Feb. 28. By isolating cancerous tumors to allow delivery of higher doses of radiation, side effects of treatment can be eliminated and survival increased, said **Gerald Hanks**, chairman of the department. . . . **LANCE ARMSTRONG FOUNDATION** and Bristol-Myers Squibb began a national cancer education Cycle of Hope campaign designed to support early detection, encouragement and advise to cancer patients and their families. Armstrong, cancer survivor and Tour de France winner, will be featured in a national public service announcement giving out the toll-free number and website to obtain an information packet (1-877-717-HOPE; http://www.cycleofhope.org. . . . **SUSUMU OHNO**, a geneticist and distinguished scientist emeritus at City of Hope Cancer Center, died Jan.13 of lung cancer. He was 71. His research contribution in the 1950's and 60's theorized that evolution occurs through duplication, rather than alteration. Ohno received the 1981 Amory Prize for Reproductive Biology. . . . **THE GROUP ROOM**, a nationally syndicated radio talk show about cancer, will hold a town-hall meeting and live remote broadcast on advances in diagnosis and treatment of colorectal cancer on March 5, 1-3 p.m. PT (4-6 p.m. ET), from the University of Southern California Norris Comprehensive Cancer Center. Guests will include Robert Beart, the Charles and Carolyn Costello Professor of Surgery at the Keck School of Medicine at USC; Heinz-Josef Lenz, assistant professor of medicine and scientific director of USC/Norris' Cancer Genetics Unit and director of its Gastrointestinal Oncology Program. Callers can enter discussions by dialing 1-800-GRP-ROOM (1-800-477-7666). To attend the event in Los Angeles, contact Michelle Rand at 818-788-5225. It will be webcast at http://www.HEALTHeatre.com.

THE CANCER LETTER

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Business & Regulatory Report

Formerly "Cancer Economics"

Oncology Management:

Aetna No Longer To Cover HDC/BMT For Breast Cancer Outside Of Clinical Trials

Aetna U.S. Healthcare, of Bluebell, PA, said that as a result of a South African investigator's admission of falsifying results of a clinical trial, the insurer will no longer cover high dose chemotherapy with bone marrow transplantation for the treatment of breast cancer outside of federally-sponsored clinical trials.

Joseph Carver, Aetna's senior medical director, said the admission earlier this month by Werner Bezwoda, of University of Witwatersrand, discredited the only clinical trial that provided evidence of the treatment's

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Clinical Trials:

BioMedicines Begins Kidney Cancer Study; EntreMed Moves Forward With Angiostatin

BioMedicines Inc. of Alameda, CA, said it has begun a phase Ib trial of the investigational drug Biomed 101 for kidney cancer.

The study will evaluate the drug candidate in combination with interleukin-2, the company said.

Clinical studies have shown that high doses of interleukin-2 can cause significant changes in blood pressure and dysfunction of the lungs, heart and kidney, the company said.

"Cancer of the kidney and metastatic melanoma are life-threatening diseases. Although interleukin-2 can be effective in such patients, when high doses are required, toxicity is often severe," said Peter Langecker, vice president of clinical affairs. "Biomed 101 is a drug intended to reduce these toxicities and to improve the tolerability and effectiveness of chemotherapy in patients."

Biomed 101 binds to the leukotriene B4 receptor. Blocking this receptor in animal models prevents adverse effects from interleukin-2. The drug candidate may have the potential to improve the tolerability and response to treatment in patients with kidney cancer, metastatic melanoma and possibly patients with AIDS, who are treated with interleukin-2, the company said.

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EntreMed Inc. (Nasdaq: ENMD) of Rockville, MD said it has received permission from FDA to begin phase I clinical testing of Angiostatin.

The first phase I trial site for Angiostatin protein will be Thomas

(Continued to page 3)

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

Aetna Ceases BMT Coverage After Bezwoda's Admission

(Continued from page 1)

effectiveness. Bezwoda said he misrepresented the treatment given to the control group in his study presented at the annual meeting of the American Society of Clinical Oncology last May (**The Cancer Letter**, Feb 11).

"With the South Africa trial discredited, there really is not good scientific evidence that this treatment is any better than combined modality treatment," Carver said to **The Cancer Letter.** "The little bit of science that was there was pulled away."

Aetna would consider covering HDC with transplantation only in the context of a clinical trial, Carver said.

"There is a clear need to try to answer what is the best course to treat breast cancer, but this can only be answered in the context of a clinical trial," Carver said. "For high dose chemotherapy, we need longer-term analyses to see if the [statistical] curves move apart.

"I honestly believe, not scientifically, but emotionally, that there are subsets where this treatment does make a difference and subsets of patients where it doesn't make a difference, and we need to learn this as soon as possible," Carver said.

Aetna began covering the treatment after the groundswell of publicity about its potential effectiveness in the 1980's and 1990's, which resulted in patient threats of legal action.

"With breast cancer, the ability to have treatment play out in a clinical trial was limited dramatically," Carver said. "We allowed people to receive high dose chemotherapy and bone marrow or stem cell transplants outside of the clinical trial world."

Carver said Aetna's statistics on the number of autologous bone marrow transplantation requests last year before and after the ASCO meeting demonstrate that the medical community has made a decision about the treatment.

From January to May, Aetna approved 105 requests and only 50 were accomplished. From June to December, after the ASCO meeting, 65 requests were approved with only 18 accomplished.

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Myriad Genetics Inc. (Nasdaq: MYGN) of Salt Lake City, said it has signed a multi-year agreement with **Kaiser Permanente** for its BRACAnalysis breast and ovarian cancer susceptibility test.

Under the agreement, Kaiser said it would offer the BRACAnalysis test throughout its system to improve the healthcare management of its 8.6 million patients.

Kaiser Permanente said it will join leading insurers and health management organizations such as Aetna US Healthcare and Empire Blue Cross and Blue Shield that have taken the lead in providing coverage for state-of-the-art medical diagnostic services to their members.

The addition of Myriad's BRACAnalysis test to the covered services provided to their members acknowledges the importance of the management of breast and ovarian cancer risk to women's health.

In another development, the company said it would provide NIH scientists and grantees with its BRACAnalysis genetic test of the BRCA1 and BRCA2 breast cancer genes as a research service.

"We are pleased that Myriad Genetics is making its BRACAnalysis molecular diagnostic test available to NIH scientists and grantees to help in further defining the role of these genes in the development of breast and ovarian cancer," said NCI Director Richard Klausner.

Klausner added that the agreement applies to genetic testing for research purposes only, not the delivery of health care services to patients.

Since the discovery of BRCA1 and high cost of

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testing DNA samples had limited the scope of the research, the company said.

Myriad and NCI created a solution that eased the financial limitations on the magnitude of the research, while providing uniform, high quality genetic testing.

Because the same test can now be used for research that is employed in clinical practice, the data from research studies can be directly applied to the care of patients, the company said.

* * *

University of Texas M. D. Anderson announced the implementation of a new academic program in health services research, part of its Division of Cancer Prevention, to define and evaluate effectiveness and efficiency of its own health services.

The program, the first of its kind to focus solely on cancer, will provide information for decision-making and policy analysis about the organization, financing and delivery of health care.

"As the range of cancer therapies grows and the funding for care is stretched thinner, patients and physicians are being forced to make tough choices every day," said Mitchell Morris, interim chairman, Division of Cancer Prevention. "There is a special need for health services research in oncology, and M. D. Anderson is positioned to develop a model program."

"In the old fee-for-service medical paradigm, there was little impetus for health services research. Health care providers had little incentive to examine the cost-efficiency of care or to respond to consumers' preferences in a non-competitive market," said Morris. "However, we now know that health services research can permit us to be competitive in the healthcare marketplace while ensuring the highest quality of care. It's a win-win situation, and thus the trend to conduct such research."

"This program has the potential to determine best practices and set a benchmark for cancer centers around the world," said Morris.

Clinical Trials:

Angiostatin Study To Begin At Jefferson University

(Continued from page 1)

Jefferson University Hospital in Philadelphia.

Walter Curran, chairman, Department of Radiation Oncology, and clinical director of the Kimmel Cancer Center in Philadelphia, and Robert Capizzi, chairman, Department of Medicine, Jefferson Medical College, will serve as co-investigators.

As with the phase I clinical trial of Endostatin protein, now underway at three sites, the phase I trial of Angiostatin protein will use a dose escalation method to determine its safety profile.

Patient enrollment is scheduled to begin this quarter upon final protocol approval from the Institutional Review Board at Thomas Jefferson University. Further information for patients and oncologists will be available through the EntreMed web site and the Thomas Jefferson University Hospital web site when patient enrollment begins.

"EntreMed successfully developed a production process for Angiostatin protein and transferred that process to large-scale GMP manufacturing at Covance in 1999, said David Jackson, vice president EntreMed Manufacturing.

"We have repeatedly produced highly potent clinical grade material in 2,000-liter fermenters, validating that EntreMed's production process is both robust and easily scalable," Jackson said.

"We were the first to clone Angiostatin protein and the first to express an active recombinant human form of the gene," said Edward Gubish, executive vice president for research and development. "Because Angiostatin protein and Endostatin protein have shown no toxicity, no evidence of drug resistance, and extraordinary safety profiles in preclinical testing, we believe they have broad therapeutic potential."

* * *

HeavenlyDoor.com Inc. (NASDAQ SmallCap: HVDC) of Cambridge, MA, and **d/b/a Procept Inc**., its biotech subsidiary, said a second NCI phase II trial has begun of 0-6-Benzylguanine chemosensitizing agent in combination with the chemotherapeutic drug carmustine for the treatment of cerebral anaplastic gliomas.

The study, at Duke University Medical Center under the direction of Henry Friedman is one of several phase II trials of the drug sponsored by NCI in colon cancer, glioma, melanoma, and sarcomas.

The trials will be conducted under a cooperative research and development agreement signed with NCI in 1998.

BG is a chemosensitizer that is designed to overcome tumor resistance to 0-6-alkylating agents. BG inactivates tumor AGT, a DNA repair protein which interferes with the effectiveness of these

agents.

Inactivation of AGT in cells is derived from 11 different human tumor types, including multiple myeloma, renders these cells more sensitive to the cytotoxic effects of several alkylating agents, the companies said.

"NCI and many investigators continue to support the clinical development of BG for a variety of cancer indications," said Nigel Rulewski, vice president, medical affairs and chief medical officer of Procept.

"In addition to multiple myeloma, brain cancer, and melanoma, Procept hopes that BG may provide increased efficacy for 0-6-alkylating agents in other cancers, such as colon, and Breast for which 0-6-alkylating agents are not commonly used," Rulewski said. "The phase 1 trials have successfully demonstrated the safety of BG, and we are eager to obtain efficacy data in phase II."

* * *

Magainin Pharmaceuticals Inc. (Nasdaq: MAGN) of Plymouth Meeting, PA, said it has begun phase II studies designed to evaluate efficacy and safety of squalamine, an angiogenesis inhibitor, for advanced ovarian cancer.

The studies are being conducted at the University of Colorado Health Sciences Center and at the Rocky Mountain Cancer Center, both of Denver, the company said.

One study will evaluate squalamine in combination with carboplatin and paclitaxel for the primary treatment of advanced ovarian cancer. The other study will evaluate squalamine in combination with carboplatin in recurrent ovarian cancer.

Magainin said it has an ongoing phase II trial evaluating squalamine for non-small cell lung cancer, the company said.

"Squalamine has demonstrated significant activity in a number of preclinical models. Therefore I am pleased to have the opportunity of evaluating its anti-angiogenic effects in patients with ovarian cancer," said Susan Davidson, lead investigator at the University of Colorado Health Sciences Center.

* * *

Novogen Ltd. (Nasdaq: NVGN; Austrialian Stock Exchange: NRT) said FDA has allowed the firm to conduct phase I trials of its drug NV-06 for prostate cancer.

The initial trial will be conducted in Sydney, Australia, and will provide preliminary pharmacokinetic and tolerability data on the intravenous form of the drug.

The results of the trial will be presented to FDA for approval for U.S. clinical trials.

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Telik Inc. of South San Francisco, a privately held company, said it has begun phase I clinical testing of TER286 in patients with advanced solid tumors or non-Hodgkin's lymphoma.

TER286 is a small-molecule cytotoxic agent that has shown activity in multiple preclinical tumor models including colon, breast, ovarian, non-Hodgkin's lymphoma, non-small cell lung cancer, and sarcoma, the company said.

The company filed its investigational new drug application with FDA in December and treated the first patient at the Jonsson Cancer Center at the University of California, Los Angeles, said Michael Wick, chairman and CEO.

"The safety and effectiveness of TER286 in preclinical models of drug-resistant tumors provides a strong rationale for this clinical trial," said Lee Rosen, director of the Cancer Therapy Development Program at the Jonsson Cancer Center and principal investigator for the trial.

Deals & Collaborations:

Aventis, MediGene In Pact For Development Of Vaccine

Aventis Pharma AG, of Frankfurt, Germany and **MediGene AG**, of Martinsried, Germany, said they have signed a licensing and development agreement for the MediGene tumor vaccine for malignant melanoma.

Under the terms of the agreement, Aventis said it has the exclusive license to develop and commercialize the vaccine in 37 countries world-wide (including the European Union, Canada, USA and Japan) with the right to grant sublicenses.

The total deal value could amount to $34 million including up-front fees, milestone payments as well as the jointly agreed R&D budget which MediGene said it will partially co-fund up to proof of concept.

MediGene said it would receive royalties on all sales as well as promotion rights for most Eastern European countries, and a number of South American, Far East and Middle East countries.

Both companies said they would be involved in the pre-clinical development and phase I/II clinical trials of the tumor vaccine. Aventis said it would be responsible for the manufacturing of the GMP material and will also conduct phase III clinical trials,

registration and commercialization of the vaccine.

"As a major player in oncology with significant expertise in the area of cell therapy and vector technologies, Aventis is an ideal strategic partner for us," said Peter Heinrich, CEO of MediGene. "The interest of this partner underlines the significance of our know-how in tumor cell processing as well as the potential of our innovative AAV-technology. In addition the promotion rights for MediGene included in the agreement allow us to implement our mid-term commercialization strategy."

* * *

Axys Pharmaceuticals Inc. (Nasdaq: AXPH) of South San Francisco, said **Axys Advanced Technologies Inc**., its combinatorial chemistry subsidiary, has entered into an agreement with **Bristol-Myers Squibb Co.,** to provide BMS with diverse compounds for pharmaceutical screening.

Axys said it would supply BMS with enabling technologies for reproducing and expanding the library chemistries. The agreement allows for payments to AAT for product delivery and technology transfer. Axys said it would terminate its collaboration with BMS to develop inhibitors to the Hepatitis C Virus protease.

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CytoGenix Inc. (OTCBB:CYGX) of Houston, said it has executed the first license for its proprietary single stranded DNA intracellular expression vector, TroVec, to **PharmaGenix LLC,** a firm owned jointly by CYGX and Professional Compounding Centers of America Inc.

TroVec is an antisense ODN delivery system. The ssDNA intracellular expression vector overcomes the delivery barrier by synthesizing sequence specific ODN antisense molecules in the cell, the company said.

The initial focus of PharmaGenix will be the development of products using nucleic acid constituents in nutritional and topical applications that are not regulated by FDA as prescription drugs, the company said.

* * *

Cytoclonal Pharmaceutics Inc. (Nasdaq: CYPH, CYPHW, CYPHZ) of Dallas said it has isolated a new class of late Taxol genes.

The company said the gene was isolated by Rodney Croteau of Washington State University, working under a contract with Cytoclonal. The genes, which represent the late steps of the paclitaxel pathway, were isolated under the company's program with **Bristol-Myers Squibb** to generate an optimized production system for Taxol using fermentation and genetic engineering.

The new class of late genes code for acyl transferases which are involved in the later part of the pathway used for the synthesis of paclitaxel, the active ingredient in Taxol, the company said. Cytoclonal signed license and research agreements with BMS in 1998 for production of paclitaxel by fermentation and genetic engineering.

* * *

Eos Biotechnology, Inc, of South San Francisco, said it has formed a multi-year alliance with **Medarex Inc.** to develop and commercialize antibody therapeutics directed at genomics-derived targets.

Eos said it would first identify and validate novel cancer antibody targets. The company said it would then use the Medarex HuMAb-Mouse technology to create fully human antibodies to those targets.

The first potential human antibody product under this alliance is expected to enter clinical trials in 2001. Eos said it would be responsible for developing the products through phase IIa trials, and said it expects to retain Medarex to perform GMP manufacturing services.

* * *

Genzyme Molecular Oncology (Nasdaq: GZMO) of Framingham, MA, said it has achieved partnering milestones from Schering-Plough Corp. and the **Parke-Davis Division of Warner-Lambert Co**., which will generate $3 million.

The payment from Schering-Plough comes from advancing its p53 tumor suppressor gene in ovarian cancer clinical trials, the company said.

Parke-Davis has renewed its license to the SAGE differential gene expression technology for an extra year with additional revenue forthcoming based on usage of the SAGE technology, the company said.

"We have had a very strong financial start to 2000. The $3 million we achieved in January is approximately two-thirds of what our total revenues were in 1999," said Gail Maderis, president, Genzyme Molecular Oncology. "P53 gene therapy represents the first therapeutic from which we could receive revenues in the form of royalties."

"SAGE is an important tool in drug discovery as pharmaceutical companies strive to develop next-generation therapies. SAGE provides essential information regarding the role of genes in disease, allowing researchers to take information from the

Human Genome Project to the next step in gene-based drug development." Maderis said.

Under the terms of the 1998 agreement with Schering-Plough, Genzyme Molecular Oncology has the potential to receive more than $30 million in additional patent, product development, and sales milestone fees, the company said.

* * *

Geron Corp. (Nasdaq:GERN) of Menlo Park, CA, said **Kyowa Hakko Kogyo Co. Ltd**. has agreed to extend its telomerase inhibition drug discovery collaboration until March 2002.

Geron said Pharmacia & Upjohn extended its telomerase inhibition discovery partnership last January, thereby maintaining the three-company alliance.

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ImmunoGen Inc. (Nasdaq: IMGN) of Norwood, MA, said it has entered into a research collaboration with the State University of New York at Stony Brook to develop novel taxane compounds which can be used as new effector molecules for the company's Tumor-Activated Prodrug (TAP) technology.

The company said it will work closely with Iwao Ojima, chairman of the Department of Chemistry. Under the agreement, joint discoveries will be owned by both parties, and ImmunoGen has an exclusive option to license SUNY Stony Brook's share.

ImmunoGen's lead TAP, huC242-DM1/SB408075, is being developed with SmithKline Beecham, and is in human clinical trials for treatment of colorectal, pancreatic and certain non-small cell lung cancers, the company said. ImmunoGen is advancing its second TAP, huN901-DM1 for treatment of small cell lung cancer. The DM1 effector molecule is a member of a family of chemotherapeutic agents called maytansinoids, which act by a mechanism similar to established chemotherapeutic drugs such as the Vinca alkaloids (e.g., vincristine, vinblastine), which inhibit tubulin polymerization. The mechanism of action of taxanes (e.g., Taxol(R), Taxotere(R)) differs from that of DM1 by inhibiting tubulin depolymerization, offering the potential to use the different TAP platforms in combination.

* * *

Kinetix Pharmaceuticals Inc. of Medford, MA, and the **Dana-Farber Cancer Institute** established a research collaboration to advance the profiling of novel anti-cancer compounds.

The collaboration seeks to evaluate the potential of small molecules to treat prostate cancer by inhibiting a target called Akt, also referred to as PKB, is a cellular enzyme that regulates apoptosis. William Sellers, of Dana-Farber, will serve as principal investigator for the project. Through the academic partnership, Kinetix will provide Dana-Farber with research funding and access to the company's portfolio of Akt inhibitors for evaluation in Sellers' cellular assays and preclinical cancer models.

"Through our work with Kinetix, we hope to further elucidate Akt's role in apoptotic and cell proliferation pathways and help in the selection of kinase inhibitors for the treatment of cancer," Sellers said. "The recent finding that the Abl kinase inhibitor, STI 571, has shown dramatic clinical responses in chronic myelogenous leukemia, validates the clinical concept of kinase inhibitors as useful cancer therapeutics."

Kinetix is a privately held biopharmaceutical company.

* * *

NeoRx Corp. (Nasdaq: NERX) of Seattle, and **PPD Inc.** (Nasdaq: PPDI) of Wilmington, NC, said they have entered into an agreement for PPD to perform phase III studies with the NeoRx skeletal targeted radiotherapy product for multiple myeloma.

The companies said PPD would provide a $5 million credit line to NeoRx to fund the trial. NeoRx will repay any principal and interest for the credit drawn, but it is under no obligation to use the credit line.

If drawn, the principal and interest is not due until the STR product is approved by FDA or abandoned by NeoRx. In return, PPD will be issued a limited number of warrants to purchase NeoRx common stock at a premium to the current price. No royalties are included.

"As our CRO during the STR clinical trials, PPD had the opportunity to observe first-hand the STR product," said Paul Abrams, CEO at NeoRx. "With their understanding of the agent and demonstrated expertise in oncology, it makes sense for us to work together on the phase III trial. With the addition of the line of credit agreement, we have secured funding for this trial in a very attractive and innovative way."

The phase III study will be a multi-center, randomized open-label trial, and is targeted to begin in the second quarter of this year. The study has been designed to demonstrate if the addition of STR to high dose therapy will increase the number of complete responses without adding significant toxicity.

The goal is to improve patient responses without increasing the side effects associated with high dose therapy. The safety profile from the phase I-II studies has led researchers to raise the age limit of study participants in the phase III study.

* * *

PPGx Inc., of Morrisville, NC, a pharmacogenomic company, said it is collaborating with **Duke University Medical Center** to study genes which may predict patient response to chemotherapy and/or susceptibility to breast cancer.

The initial collaboration will focus on single nucleotide polymorphisms in genes that are involved in the metabolism of drugs used in high dose chemotherapy regimens, the company said.

Scientists from both organizations will identify and screen candidate genes for SNPs in their DNA sequences looking for genetic markers that predict efficacy and safety factors in high dose chemotherapy regimens for high risk and advanced stage breast cancer.

The scientists will validate new SNPs as genetic markers in drug target, pathway and disease genes that may be implicated in advanced stage breast cancer, the company said.

Product Approvals & Applications:

Firm To Study Imaging System As Adjunct To Mammogram

Computerized Thermal Imaging Inc. (CTI-OTC Symbol:COII) of Layton, UT, said it is seeking pre-market approval from FDA for its Computerized Thermal Imaging System as an adjunctive diagnostic test to the mammogram and clinical examination for the detection of breast cancer.

The CTIS uses a heat sensitive camera to record thermal images of breast tissue, which are processed by proprietary computer algorithms. The test is simple, painless and involves no radiation, breast compression, electrodes or electrical current, the company said.

* * *

Enzon Inc. (NASDAQ: ENZN) of Piscataway, NJ, said FDA has accepted the biologics license application for **Schering-Plough Corp.'s** (NYSE: SGP) PEG-Intron for the treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease.

PEG-Intron is a modified form of Intron A (interferon alfa-2b) that uses proprietary PEG technology.

"We have always assumed that PEG-Intron would receive the standard 12-month FDA review," said Peter Tombros, president and CEO of Enzon. "Schering-Plough has to be commended for the speed at which they have conducted their clinical trial program."

In Europe, Schering-Plough has submitted a centralized marketing authorization application for PEG-Intron to the European Union European Agency for the Evaluation of Medicinal Products seeking marketing approval for the same indication.

* * *

ILEX Oncology Inc. (Nasdaq: ILXO) of San Antonio, TX, said FDA has accepted its biologics license application and given orphan drug designation for Campath (alemtuzumab).

Campath, an investigational humanized monoclonal antibody, received Fast Track designation from FDA and is expected to undergo a six-month priority review under the Prescription Drug User Fee Act, the company said.

* * *

Ligand Pharmaceuticals Inc. (Nasdaq: LGND) of San Diego, said FDA has accepted the new drug application for Targretin (bexarotene) gel 1%, for priority review.

Targetin gel 1% is a topical therapy for cutaneous lesions in patients with stage IA, IB or IIA cutaneous T-cell lymphoma who have not tolerated other therapies or who have refractory or persistent disease, the company said.

"We are prepared to work closely with FDA to facilitate its review to make Targretin gel available to patients as soon after approval as possible," said David Robinson, Ligand chairman, president and CEO.

Ligand said it is targeting submission of a marketing authorization application with the European Agency for the Evaluation of Medicinal Products for Targretin gel.

In June 1999, FDA granted orphan drug designation to Targretin for the treatment of patients with CTCL and, in December, approved the capsule formulation of Targretin for the treatment of cutaneous lesions of patients with early- and advanced-stage refractory CTCL.

Last November, Ligand submitted an MAA for Targretin capsules for the treatment of patients with CTCL.

Ligand said it is currently conducting phase II

trials with Targretin capsules for the treatment of patients with moderate to severe plaque psoriasis and for the treatment of women with advanced breast cancer.

* * *

Novartis Pharmaceuticals Corp., of East Hanover, NJ, said Zometa (zoledronic acid for injection), an investigational treatment for tumor-induced hypercalcemia, has been designated for priority review by FDA.

The NDA filing was based on clinical data derived from two identical studies comparing Zometa to Aredia (pamidronate disodium for injection), another Novartis agent.

In the studies, the combined results demonstrated that a statistically significant higher percentage of patients responded to Zometa 4 mg (88.4 percent) versus Aredia (70 percent) in reducing serum calcium levels to the normal range. Zometa was infused over 5 minutes, while infusion times with Aredia TIH can range from four to 24 hours, the company said.

* * *

SICOR Inc. (Nasdaq: SCRI) of Irvine, CA, said **Gensia Sicor Pharmaceuticals Inc**., its subsidiary, has received approval of an Abbreviated New Drug Application from FDA for Daunorubicin Hydrochloride Injection and for Fluorouracil Injection USP.

Daunorubicin is used in the remission induction in acute myelogenous leukemia in adults and acute lymphocytic leukemia in children and adults. Fluorouracil is effective in the palliative management of carcinoma of the colon, rectum, breast, stomach and pancreas, the company said.

* * *

SuperGen Inc. (Nasdaq: SUPG, SUPGW, SUPGZ) of San Ramon, CA, said the Therapeutics Products Programme of Canada has approved an investigational new drug submission for rubitecan, an anticancer compound.

SuperGen said clinical trials of rubetican would begin in Canada.

Rubitecan is an oral chemotherapy compound in the camptothecin class and is currently in late-stage phase III studies at more than 200 clinical sites worldwide for the treatment of pancreatic cancer, the company said.

Because rubitecan showed pre-clinical activity in a number of different cancers, clinical studies have begun for a variety of solid tumors and hematological malignancies, the company said.

In another development, the company said it has been issued U.S. Patent No. 6,017,948, covering water-miscible formulation of Taxol (paclitaxel, Bristol Myers-Squibb).

The current formulation of Taxol is a non-aqueous solution containing Cremophor EL (polyoxyethylated castor oil) and alcohol. Patients need to be pre-medicated prior to administration, so that they are able to tolerate a non-water-miscible, potentially toxic formulant.

The current formulation may attack and corrode plasticized PVC equipment or devices used to prepare infusions for patients. SuperGen said its formulation addresses these problems.

* * *

UroMed Corp. (NASDAQ SmallCap: URMD) of Norwood, MA, said FDA has cleared for U.S.marketing and distribution its CaverMap Surgical Aid. The aid is used during prostate surgery to identify and spare sensitive nerves for erectile function.

Patents:

Techniclone Wins Patent For Tumor Necrosis Therapy

Techniclone Corp. (NASDAQ:TCLN) of Tustin, Ca, said its Tumor Necrosis Therapy technology has been issued US Patent #6,017,514 for the treatment and diagnosis of solid tumors.

Techniclone said the patent allows the use of TNT, based on the principle that all solid tumors build poor vascular networks and eventually outgrow their blood supply leading to the development of a core of dead and dying tumor cells, as an imaging agent to determine the effectiveness of conventional cancer therapy.

According to the patent, a labeled TNT antibody is used to obtain an initial image of the tumor. Following a course of therapy, another TNT image of the tumor is obtained. If the cancer therapy has been successful, the post-therapy image should show increased areas of necrosis. If the therapy has not been successful, the post-therapy image will appear much like the initial image.

Techniclone said this use of TNT may make it possible for physicians to make an earlier estimate of the effectiveness of a given treatment regimen. This would allow the physician more quickly to switch to alternative treatment options should the initial treatment be ineffective, the company said.

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