THE CANCER LETTER INTERACTIVE

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Advisors Approve NCI Plan To Contract For Early Clinical Trials Of Imaging Agents

Adding another building block to NCI's emerging infrastructure for validating molecularly-targeted therapeutics, the NCI Board of Scientific Advisors approved the Institute's plan to establish a new contract program for phase I and phase II clinical trials to rapidly evaluate new imaging probes, ligands, radiopharmaceuticals, and contrast agents.

NCI proposes to spend more than $22 million over five years, starting in fiscal 2001, to support a total of 56 trials in molecularly-targeted imaging.

The contract program is needed to test several new imaging agents that are in development through NCI grants, Institute officials said. These

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In Brief:

NCI Recruits Carl Barrett Of NIEHS To Direct Basic Sciences; Freedman Named To NCAB

CARL BARRETT, scientific director of the National Institute of Environmental Health Sciences since 1995, has been appointed director of the NCI Division of Basic Sciences effective April 9. Barrett, a molecular geneticist, has been chief of the Laboratory of Molecular Carcinogenesis at NIEHS since 1987. He is an expert on mismatched repair genes and telomerase. He received a B.S. in chemistry from William and Mary College, and Ph.D. in biophysical chemistry from Johns Hopkins University. He has worked at NIEHS since 1977. Barrett replaces **George Vande Woude**, who left the Institute last October. NCI Deputy Director **Alan Rabson** has served as acting director of the division for the past six months. . . . **RALPH FREEDMAN**, of Houston, a gynecologist and professor of gynecologic oncology at the University of Texas M.D. Anderson Cancer Center, was appointed by **President Clinton** to the National Cancer Advisory Board, the White House said earlier this week. Freedman also is a professor of obstetrics, gynecology, and reproductive sciences at the University of Texas Houston Medical School. He has worked as a medical consultant for numerous agencies and commissions, including the World Health Organization, NCI, and NASA. Freedman received his medical degree and Ph.D. from the University of the Witwatersrand in Johannesburg, South Africa. . . . **SUSAN SIEBER** has been named Director of Communications for NCI, heading a new Office of Communications, which replaces the Office of Cancer Communications. The reorganization, which has yet to be officially announced, was approved by the NCI Executive Committee in late

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BSA Approves $22 Million Early Trials Contract Program

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agents soon will require clinical validation, and most academic investigators do not have resources for these trials.

The funding would support up to 30 phase I safety trials, and 26 would be phase II efficacy trials over five years. Phase I trials would involve about 10 patients each at one or two institutions. Phase II studies would enroll about 25 to 75 patients at two or more institutions.

Competitive contracts would be awarded to five institutions to conduct the trials. "Ad hoc" sites for trials may be added as needed, either through competitive or sole source funding.

Following is the edited text of the concept statement:

Early Clinical Trials of Imaging Agents. Concept for a new Request for Proposals. Proposed funding: FY01 $1.69 million; FY02 $3.28 million; FY03 $4.87 million; FY04 $6.09 million; FY05 $6.09 million. Project officer: Anne Menkens, Biomedical Imaging Program, Molecular Imaging Branch, Division of Cancer Treatment and Diagnosis, phone 301-496-9531, e-mail: am187k@nih.gov.

The contracts will create an early clinical trials infrastructure to rapidly evaluate molecularly-targeted imaging probes, ligands, radiopharmaceuticals, and contrast agents to assess anticancer agents on their molecular targets and determine clinical relevant correlates.

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The objectives of this program are: to rapidly conduct clinical trials necessary to assess the safety and imaging capabilities of promising imaging agents; to characterize the molecular interactions of new molecular imaging agents with their targets through biopsies, assays, and other appropriate technologies and correlate those effects with clinically relevant endpoints; and to develop new scientific insights into molecular pathways and dterminants of the relationship of the targeted imaging agents to therapeutic drug response.

BIP estimates a need to evaluate approximately 10 to 20 promising imaging agents per year. However, we suggest starting with a smaller number and gradually increasing over four years Since this is a new program, for which there is no precedent, it is difficult to accurately gauge the demand and number of agents that we will find compelling to support. For the initial evaluation of safety, we propose that this initiative fund eight single institution trials per year, for each of three successive years, and then 10 safety trials for years 4 and 5 of this program. A total of up to 10 patients per trial will be funded.

In year two, we propose that four preliminary clinical efficacy trials be funded. This would increase to eight in year 3 and 10 in years four and five. A maximum of 25 patients per trial will be funded.

The increasing schedule proposed above adds up to 8 contracts in year 1, 12 in year 2, 16 in year 3, and 20 in years 4 and 5.

These contracts will require rapid implementation and completion of trials and they will require the ability to implement correlative studies validating the localization of the investigational imaging agents on their molecular target in tumors. Some imaging agents will originate from investigators not affiliated with clinical sites. Such investigators will likely be willing to work with NCI to place their agent in clinical trials at standing contract sites to be selected by the process described below. Other agents will originate at sites that do have the capability to perform clinical trials and the discoverer will want to perform the clinical trials at his or her site.

We therefore propose that this initiative provide funds to carry out trials either at standing contract sites or by sole-source contracts when that is most appropriate. Support is requested for testing a total of eight to 20 imaging agents, and for purposes of beginning this program, we estimate that half would be tested at standing contract sites and half at the discoverers' sites (i.e., sole-source contracts). For imaging agents that would be tested at standing contract sites, we estimate that a pool of approximately 5 contract sites will be required.

For all clinical trials, whether at standing contract sites or at the inventor's site, the BIP will expect the contractor to include in his/her cost per patient the cost of procedures and assays directly tied to the evaluation of the clinical endpoints (e.g., pharmacokinetic studies) and correlative studies characterizing the new imaging

agents on their targets. The BIP will expect the contractor to fund within the patient study the costs of personnel time, imaging procedures, laboratory studies, and procedures directly related to the laboratory correlative investigations. Each of the clinical trials will have at least one correlative laboratory investigation (to validate the agent's clinical role), for a total of a maximum of 20 laboratory correlative studies per year.

Because the agents involved will require FDA approval, contractors must be familiar with the requirements of validation of imaging agents as outlined by FDA. These requirements are currently under revision but will be important in the design and implementation of safety or preliminary clinical efficacy trials of promising imaging agents.

For the standing contracts, BIP will formulate the request for proposals in conjunction with the Research Contracts Branch of NCI. The initial peer review will be administered through NCI. It is anticipated that approximately five contract sites will be chosen. For these standing contracts, the Request for Proposals will solicit single institutional arrangements of clinicians, statisticians, data managers, and research nurses from academic institutions or industry with early phase clinical trial expertise with investigational imaging agents. Offerors for these contracts must demonstrate that they have expertise in molecularly targeted imaging agent development and performance of safety or preliminary clinical efficacy trials of imaging agents. They need to provide evidence of their own expertise, or access to such expertise, in diagnostic, molecular, or metabolic imaging, interventional radiology, pathology, and other potentially relevant laboratory methodology. Each contract applicant needs to show evidence of sufficient numbers of patients or normal control subjects to be able to conduct clinical trials using targeted imaging probes, ligands, radiopharmaceuticals, or contrast agents in at least one imaging modality but preferably several modalities. Proposals for sole-source contracts will need to demonstrate similar expertise and resources relevant to the imaging agent being proposed for study.

The safety trials will be designed to test safety and determine the appropriate amount of the targeted imaging agent that provides acceptable image quality. The size of each trial might vary depending on consultation with FDA for each specific agent. The typical size for each safety trial will be approximately 10 patients. The typical size of each preliminary clinical efficacy trial is estimated to be 25 patients.

For common tumors such as breast, colon, prostate and lung, studies must take no more than one year from approval of a Letter of Intent to completion of accrual. For less common tumors, studies should be completed no more than 18 months after LOI approval. To ensure efficient conduct of studies, full contract credit will not be given unless patients are accrued and trials completed in the time specified, with the quality of the data assured. Quarterly progress reports on accrual will be reported to BIP, and payment will be based on the quarterly numbers of patients accrued. Contract payments will be made on a work-completed basis.

Applications should include a description of previous experience with imaging agent clinical trials, correlative studies, and a description of data management and analysis experience. A thorough analysis of patients and normals (including demographics and various types of malignancies) available to participate in clinical trials of imaging agents must be well documented. Description of imaging technologies and the quality assurance issues related to the modalities, available laboratory facilities for clinical trials including patient monitoring studies (i.e., pharmacokinetics, immune response, etc) or clinical correlative studies should be specifically addressed. Specific steps that will be taken to assure adherence to FDA recommendations and guidelines for Safety and Preliminary Clinical Efficacy testing of imaging agents must be explicitly documented.

After the successful standing contractors are identified, the BIP will, on an as-needed basis, call for solicitation of proposals to conduct clinical trials with IND-approved agents from NCI, academia, or industry. The previously selected standing contractors will submit a letter of intent to conduct the trial. The trial site(s) will be chosen by an NCI-coordinated process that will include internal review by NCI staff and external ad-hoc expertise as needed. An LOI may be rejected, approved with the requirement for recommendations to be incorporated, or fully approved. Upon approval of the LOI, the successful contractor will write the final clinical protocol within 30 days, and NCI staff will review this protocol within 30 days. After protocol approval, the contractor will have up to one year or some deadline mutually agreed upon by the BIP project officer and the contractor, to complete the trial.

Board Tables Outcomes Research Concept

The NCI Board of Scientific Advisors voted to table a concept proposal titled "Population-Based Cancer Care and Outcomes Research Consortium," presented at its meeting last week by the Division of Cancer Control and Population Sciences.

The board formed a subcommittee to work with NCI staff to revise the concept, which will be scheduled for presentation to the board at its meeting in June.

The concept proposed to set aside $45 million over five years to fund 10 to 14 cooperative agreements for large, observational cohort studies in breast and colorectal cancer to identify the components of high quality cancer care.

Board members said they were concerned about the feasibility of the proposed research.

NCI Programs:

"5 A Day" Review Underway To Check Program's Health

NCI has formed a committee to evaluate the national 5 A Day for Better Health program that seeks to encourage greater consumption of fruits and vegetables, an Institute official said last week.

Robert Croyle, associate director for behavioral research in the NCI Division of Cancer Control and Population Sciences, said the Institute would like the evaluation panel to review whether the goals of the program have been achieved, the quality of science, NCI's role in the program, and the implications for priorities in behavioral research.

As a research institute, NCI's role in health promotion programs is "politically controversial," Croyle said in a presentation March 24 to the NCI Board of Scientific Advisors. The formation of the evaluation panel has raised the concern of the fruit and vegetable industry organizations that have helped promote the program, Croyle said. Croyle said he has tried to assure those involved that program reviews have become an established part of the NCI's planning process.

"The review is not being done because we don't have an interest in 5 A Day, but as part of the NCI priority-setting process," Croyle said.

The industry spends an estimated $30 million to $50 million primarily through in-kind services to promote 5 A Day, Croyle said.

The 5 A Day program began in 1991 as a collaboration between NCI, the Produce for Better Health Foundation, and the Centers for Disease Control and Prevention. NCI set aside $16 million to fund community-based research grants for 5 A Day between 1993 to 1996. Nine grants were funded from the original Request for Applications.

The Institute has spent a total of $40.41 million since FY92 on 5 A Day, including the original $16 million in grants, according to budget figures NCI provided to **The Cancer Letter**.

In FY99, NCI spent $7.5 million on the program, including $1 million on communications, $5.6 million on nutrition and behavioral change research, and $150,000 for program evaluation. The budget also included $650,000 that NCI provided CDC for state health agency evaluation research of state 5 A Day interventions.

The evaluation panel held its first meeting in January, and has scheduled a second meeting for April. The group plans to submit a written report to the BSA in November.

John Potter, head of the Cancer Prevention Research Program at Fred Hutchinson Cancer Research Center, will serve as chairman of the panel. Panel members are: Leonard Epstein, professor, departments of pediatrics, social and preventive medicine, and psychology, State University of New York at Buffalo; John Finnegan Jr., associate professor and associate dean for academic affairs, University of Minnesota School of Public Health; Elmer Huerta, director, Cancer Risk Assessment and Screening Center, Washington Cancer Institute; Jean-Xavier Guinard, associate professor of science and technology University of California, Davis; Steve Kelder, associate professor, University of Texas, Houston Health Science Center; Alan Kristal, associate head, Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center; Shiriki Kumanyika, associate dean for health promotion and disease prevention, University of Pennsylvania School of Medicine; Ruth Zu-Kei Lin, oncology clinical nurse, Morristown Memorial Hospital, NJ; Brenda McAdams Motsinger, head, Health Promotion Branch, Division of Public Health, North Carolina Department of Health and Human Services; Franklyn Prendergast, director, Mayo Foundation, Mayo Cancer Center; and Glorian Sorensen, director, Center for Community-Based Research, Dana-Farber Cancer Institute. Executive secretary of the committee is Kevin Callahan, deputy director, NCI Office of Science Planning and Assessment.

5 A Day Recipes

Americans are consuming more fruits and vegetables since the 5 A Day program began, according to NCI. On average, adults consume 4.4 daily servings and children consume 3.9 daily servings. A serving is defined as: one medium piece of fruit; 1/2 cup of fruit or vegetables; one cup of leafy salad greens; 1/4 cup of dried fruit; 3/4 cup or six ounces 100% fruit juice; 1/2 cup cooked or canned dried peas or beans.

In time for the NCAA "final four" basketball championship games April 1-3, the 5 A Day program released new recipes for soups and dips—all low in fat and sodium, and easy to prepare, according to the Institute. The new recipes are posted at http://dccps.nci.nih.gov/5aday/new.html. The program maintains a Web site at http://5aday.gov/.

Professional Societies:

AACR Honors Nine Cancer Researchers, Clinicians

The American Association for Cancer Research will honor nine cancer investigators with its annual research awards and lectureships at the association's 91st meeting in San Francisco, April 1-5.

The AACR Pezcoller International Award for Cancer Research will be presented to Charles Sherr, chairman and Herrick Foundation Chair, Department of Tumor Cell Biology, St. Jude Children's Research Hospital, and investigator, Howard Hughes Medical Institute. Sherr is being honored for his contributions to the understanding of the mechanisms of cell growth control and neoplastic transformation.

The 2000 G.H.A. Clowes Award will be awarded to Elizabeth Blackburn, professor, departments of biochemistry and biophysics and of microbiology and immunology at the University of California at San Francisco for her discovery of telomerase and its potential role in cancer treatment and aging.

Edison Liu director, Division of Clinical Sciences at NCI, will receive the Richard and Hinda Rosenthal Foundation Award for his translational research using oncogene markers for therapeutic selection in the areas of signal transduction and pathways in breast cancer.

The Joseph H. Burchenal AACR Clinical Research Award will be presented to Wuan Ki Hong, professor and chairman, American Cancer Society Clinical Research Professor, Charles A. LeMaistre Distinguished Chair in Thoracic Oncology, Department of Thoracic/Head and Neck Medical Oncology, M. D. Anderson Cancer Center, for his contributions to clinical cancer research and patient care in the areas of head and neck and upper airway malignancies.

Nikola Pavletich, member, Cellular Biochemistry and Biophysics Program, Memorial Sloan-Kettering Cancer Center is the recipient of the Cornelius P. Rhoads Memorial Lecture. Pavletich is being honored for his contributions to structural biology in the areas of proteins involved in growth control and cancer, and cell cycle regulation.

The DeWitt S. Goodman Lecture will be awarded to John Potter, head, Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center. Potter is being honored for his contributions to cancer epidemiology and diet, nutrition, and cancer prevention research.

The Bruce F. Cain Memorial Award will be presented to Axell Ulrich, director, Department of Molecular Biology, Max-Planck-Institute for Biochemistry, Martinsried, Germany. The award honors Ullrich for his contributions in the identification and pharmaceutical exploitation of tyrosine kinase receptors and their ligands.

Walter Willett, Frederick John Stare Professor of Epidemiology and Nutrition, and chairman, Department of Nutrition, Harvard School of Public Health, is the recipient of the AACR American Cancer Society Award for research excellence in cancer epidemiology and prevention. Willett is being honored for his contributions to the field of diet and health.

The third AACR-Women in Cancer Research Charlotte Friend Memorial Lecture will be awarded to Leona Samson, professor of toxicology, Harvard School of Public Health, for her accomplishments in cancer research. Her achievements include the exploration of basic mechanisms of spontaneous mutagenesis and alkylation-induced mutagenesis; gene therapy approaches for protecting cancer patients against bone marrow toxicity during chemotherapy; and how the transcription of certain genes is modulated when cells experience DNA damage.

Funding Opportunities:

NCI Pre-Solicitation Notice For Molecular Target Labs

Over the past decade our understanding of the molecular basis of cancer has increased dramatically. Exploiting technological advances, NCI has established interdisciplinary programs, such as the Cancer Genome Anatomy Project, to put in place technology, physical resources, and information to allow deciphering of the molecular anatomy of a cancer cell. The cancer research community now has access to large collections of genes, which represent the majority of all human genes, and is utilizing these resources most effectively to classify cancers at the molecular level. These advances have occurred in parallel with evolutionary changes in the ability to synthesize highly diverse collections of compounds, manipulate genetic sequences, and perform biological screens in a more precise and high-throughput manner.

New approaches and advances in imaging technology and bioinformatics have enabled a fundamental re-conceptualization of the process of discovery. The expected result is a more precise understanding of the roles

that genes and networks of genes (and their products) play in various aspects of cancer development, thereby enabling new approaches to cancer intervention.

In order to empower the research community to fully exploit this remarkable new opportunity, the NCI intends to establish Molecular Target Laboratories (MTLs) to mount an intensive program of ligand discovery for cancer-related targets. The immediate benefits of ligand identification will be a resource of chemical probes for biological studies of cancer, including physiological and biochemical monitoring. In addition, it is expected that the resources generated by this program will build a platform for drug discovery, and for imaging resource construction.

More specifically, the ultimate products of the MTLs are envisioned to be:

—Chemical libraries: will constitute the principal sources of chemical diversity to be interrogated by the biological assays developed in the MTLs. The 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, SAIC and the 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.

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

—Information: the identification of biologically active small molecules and the relationship of particular chemical structures to biochemical activity and cellular phenotype. This information will be made publicly available expeditiously and systematically. To accomplish this goal, the MTLs will work with SAIC and the 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 intellectual property review. This database will also incorporate data from other qualified research groups in the cancer research community wishing to participate. NCI envisages that it will, in time, serve a role for ligand discovery efforts analogous to that of DNA sequence databases for gene discovery.

In order to achieve the scientific objectives of NCI each MTL shall have expertise and capability in chemistry, biology, and the integration of biological and chemical resources:

1) Chemistry

* design, synthesize, store and format chemical libraries

* perform chemical synthesis including structural modification, as well as the ability to scale-up synthesis

* design and implement biological, synthetic, or biochemical screens

2) Biology

* provide expertise in cancer biology

* develop assays suitable for screening

* perform biological studies for probe validation and target identification

3) Integration

* design and operate high-throughput screens on selected targets

* evaluate the imaging potential of selected probes

* provide informatics know how and resources for effective project management, to make MTL resources accessible to the research community, and to participate in the development of a public database relating chemical structure to biological function

* produce and distribute resources to the community

* provide an independent business management system to support MTL activities

To meet the special needs of this scientific program, NCI will provide funding through a contract to Science Applications International Corp. (SAIC), the operator of a Federally Funded Research and Development Center, for the establishment of the MTLs. This is intended to be a multi-year program with an initial one-year contract and multiple option years. It is anticipated that up to two awards will be made.

NCI wants to ensure that new technologies that may be developed by MTLs under this contract are made available, as much as possible, to the research community for further research and development. It is anticipated that this will more rapidly and effectively lead to products of benefit to the public.

NIH recognizes the rights of contractors/subcontractors normally to elect and retain title to subject inventions developed with federal funding under the provisions of the Bayh-Dole Act. However, to address the government's present interest in the availability of the new technology developed under this Contract, the NIH is invoking the provision of the Bayh-Dole Act at 35 U.S.C. § 202 (a)(ii) 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]".

Therefore, respondents are advised that a Determination of Exceptional Circumstances (DEC) along with the associated deviated FAR clauses will be used for this Initiative. The respondents should note that the DEC will enable the NCI to either elect title to inventions developed by the MTL under this Initiative, or to grant greater rights to such inventions to the MTL. The finalized version of the deviated FAR clauses will be available before final award of any potential contracts.

A pre-solicitation conference has been scheduled

for April 19th to further discuss the goals of this initiative, IP issues and DEC guidelines and considerations. Further details and a registration form are available at http://www.ncifcrf.gov/mtl. A draft solicitation will be available by contacting Heather Wells at phone: 301-846-1520 or via. fax: 301-846-5414.

Potential offerors are invited to submit questions prior to the pre-solicitation conference. Questions received will be addressed in the final solicitation.

Program Announcements

PA-00-080: Molecular Epidemiology of Prostate Carcinogenesis

NCI, National Institute of Diabetes and Digestive and Kidney Diseases, and the National Institute of Environmental Health Sciences invite investigator-initiated research grant applications of molecular epidemiologic studies for prostate cancer development and progression.

The purpose is to stimulate development and application of biological markers of prostate cancer risk and tumor aggressiveness and for utilization in chemoprevention studies. Of special interest are studies of markers to elucidate multiethnic differences in prostate cancer susceptibility. The mechanism of support will be through individual research project grants R01.

Inquiries: Kumiko Iwamoto, NCI, Executive Plaza North, Suite 535, Bethesda, MD 20892-7395, phone 301-435-4911, fax 301-402-4279; e-mail ki6n@nih.gov

PA PAR-00-079: Improving DNA, RNA and Protein Availability in Fixed Tissue

Letter of Intent Receipt Dates: June 14, 2000 and Feb. 9, 2001

Application Receipt Dates: July 19, 2000 and March 16, 2001

NCI believes a better understanding of the physical and chemical basis of tissue preservation is vital for the rational development of new fixation methodologies. The initiative would encourage research to develop (1) new fixation methods to better preserve macromolecules and (2) methods to reverse the effects of formalin fixation to make nucleic acids and proteins more readily accessible in archived specimens. The PA will use the NIH exploratory/developmental R21 grant mechanism.

Inquiries: Marianna Bledsoe, Division of Cancer Treatment and Diagnosis, NCI, Executive Plaza North, Room 700, 6130 Executive Blvd, Bethesda, MD 20892-7399, Rockville, MD 20852 (for express/courier service), phone 301-496-7147; fax 301-402-7819; e-mail mb80s@nih.gov

PA: Development of Novel Imaging Technologies: SBIR/STTR Initiative

The initiative is intended to facilitate the development of novel imaging technologies for early cancer detection, screening, diagnosis and image guided treatment through (a) the development of highly innovative image acquisition and enhancement methods, including high risk/high gain technologies that exploit our expanding knowledge of the molecular basis of cancer, and (b) the integration of these emerging and more traditional technologies for more effective solutions for cancer.

Inquiries: Barbara Croft, Biomedical Imaging Program, DCTD, NCI, phone 301- 496-9531; e-mail: bc129b@nih.gov

PA PAR-00-076: Grants for Health Services Dissertation Research

Application Receipt Dates: May 5, 2000, Sept. 15; Jan. 15; May 15; annually

Agency for Healthcare Research and Quality announces the health services dissertation research small grant program undertaken as part of an academic program to towards a doctorate.

To qualify, the student must be enrolled in an accredited research doctoral degree program in health services research, including areas such as social, behavioral, biostatistical, epidemiological, economic, educational, policy, management, medical, nursing, or health sciences, which require a dissertation based on original research.

The PA will use the small research grant R03 mechanism of support.

Inquiries: Dissertation Program Specialist, Division of Research Education, Office of Research, Review, Education, and Policy, Agency for Healthcare Research and Quality, 2101 East Jefferson Street, Suite 400, Rockville, MD 20852-4908, phone 301-594-1449; e-mail training@AHRQ.gov

RFA Available

RFA: Pre-In vivo Cellular and Molecular Imaging Centers (Pre-ICMICs)

This initiative seeks to establish Pre-In Vivo Cellular and Molecular Imaging Centers for in vivo cancer imaging. Pre-ICMICs are designed to provide institutions with an organizational structure to facilitate new interdisciplinary collaborations, and the resources to initiate developmental projects focused on the molecular imaging of cancer. Such multidisciplinary Pre-ICMICs would stimulate and streamline cancer-imaging rsearch from inception to use in patient care.

Inquiries: Anne Menkens, Diagnostic Imaging Program, Division of Cancer Treatment and Diagnosism, NCI, phone 301-496-9531; e-mail am187k@nih.gov

NCI Contract Awards

Title: Resynthesis of Compounds for Preclinical Development

Contractor: Starks Associates Inc, Buffalo, NY, $1,247,542

In Brief:

Sieber Directs Communications At NCI, Reorganizing Offices

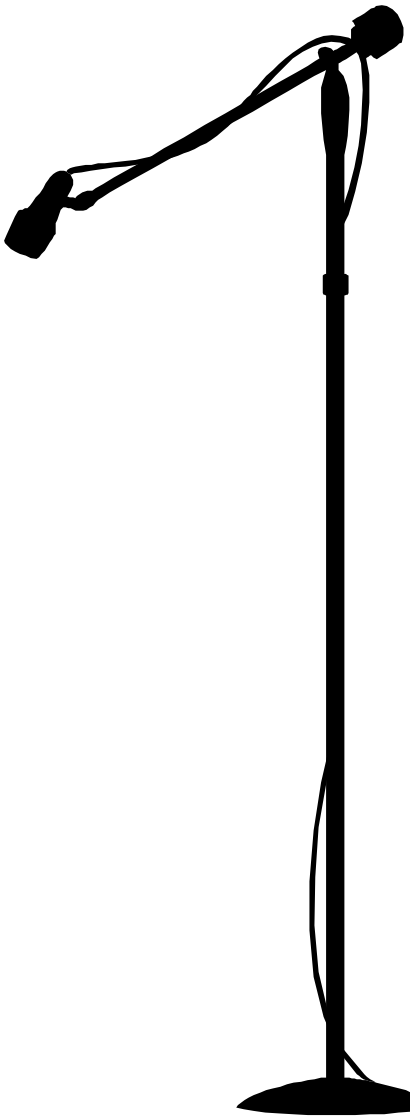
(Continued from page 1)

January. The office will include five programs, each headed by an associate director: Electronic Information Products and Systems; Communications Coordination; Outreach and Partnerships; Media and Public; and Technologies and Services. Recruitment for the five associate director positions was to begin in March and conclude by July. The reorganization is scheduled to be completed by September. The "operating principles" of the new office: "To integrate NCI's communications activities so that the Institute speaks with one voice. To ensure that NCI's messages are presented in a scientifically valid and understandable fashion and are culturally appropriate. To establish a framework for dealing with issues proactively and with a structured, formalized team approach. To provide an infrastructure to facilitate NCI-wide communication activities. To ensure and promote the NCI brand across the Institute. To establish and maintain partnerships with other government entities, professional organizations, and patient/consultant groups. To enhance internal NCI communications. To integrate new technologies throughout communications activities." NCI Executive Committee meeting minutes are posted at http://camp.nci.nih.gov/admin/boards/ec/dir.htm. . . . **SCOTT LEISCHOW**, an expert in pharmacological treatments for nicotine research, has been appointed chief of the NCI Tobacco Control Research Branch in the Behavioral Research Program effective July 2. Leischow is director of the Arizona Program for Nicotine and Tobacco Research, co-director of the Biobehavioral Oncology Research Program at the Arizona Cancer Center, and associate professor, School of Public Health, University of Arizona in Tucson . . . . **SEN. CONNIE MACK** (R-FL) was honored by the Association of Community Cancer Centers with its Annual Achievement Award for his contributions to cancer care. "Throughout his career in congress, Senator Mack has made patient access to state-of-the-art cancer care, prevention, screening, early detection, patient rights, and cancer research top priorities in Washington, DC," said Margaret Riley, outgoing ACCC president. Mack, a melanoma survivor, serves on the Senate Finance Committee and co-chairs the Senate Cancer Coalition with Sen. Diane Feinstein (D-CA) . . . . **FOX CHASE CANCER CENTER** and **JEFFERSON MEDICAL COLLEGE** of Thomas Jefferson University received a $2.4 million contract from NCI to evaluate potential cancer prevention agents. The project will use the new DNA microarray technology to study the affects of cancer agents on cells containing altered human genes associated with hereditary cancer risk. Alfred Knudson, Lasker Award winner and Fox Chase distinguished scientist, is principal investigator. Bruce Bowman, director of medical oncology and medical genetics at Jefferson, and an expert in hereditary and non-hereditary colon cancer, is co-director of the Jefferson portion of contract. . . . **ELIZABETH McCORMICK** was appointed executive director of nursing at Memorial Sloan-Kettering Cancer Center. She will oversee a nursing staff of more then 950 and will be responsible for inpatient and outpatient care at Memorial facilities in Manhattan and its regional sites. McCormick was vice president of the Allen Pavilion, New York Presbyterian Hospital and director of Administrative and Ambulatory Nursing Programs and director of Critical Care Nursing at New York Hospital-Cornell Medical Center. . . **RICHARD THERIAULT**, a breast medical oncologist and professor of medicine at M.D. Anderson Cancer Center, was appointed vice president for medical affairs for the M.D. Anderson Outreach Corporation and the M.D. Anderson Physicians Network. Theriault is responsible for medical support for the center's business development activities. He will assist Martin Raber, senior vice president for strategic and business planning and serve as liaison for the cancer center Clinical Council and Physicians Referral Service Management Team. . . . **BIOTECHNOLOGY INDUSTRY** leaders at the BIO 2000 International Biotechnology Meeting and Exhibition announced the establishment of the **Robert A. Swanson** Education Fund to honor the founder of Genentech and biotechnology industry pioneer who died last December. Contributions may be made to the non-profit administrator of the fund: Biotechnology Institute, Robert A. Swanson Education Fund, 1625 K St., NW, Suite 1100, Wash., DC, 20006 . . . . **GENENTECH INC.** received the 2000 Helix Award at BIO 2000. The excellence award for the international biotechnology industry, sponsored by the State University of New York at Stony Brook Center for Biotechnology, honors corporate leadership in the areas of scientific innovation, company growth and corporate citizenship.

Announcing the

John R. Durant ROAST

benefitting the John R. Durant Fund for Cancer Communications



A TRIBUTE TO ASCO LEADERSHIP

The National Coalition for Cancer Survivorship (NCCS) is honored to host the official roast of John R. Durant, MD, retiring Executive Vice President of the American Society of Clinical Oncology (ASCO).

Through the stories of his colleagues and close associates, we will look back on the many achievements of Dr. Durant, and have a wonderful time roasting our friend. By uniting leaders in cancer care to recognize Dr. Durant's contributions to cancer research, treatment and survivorship, we will also honor current ASCO leadership who will ensure that his vision and good work continue.

Proceeds from this roast will be used to establish The John R. Durant Fund for Cancer Communications.

May 20, 2000

New Orleans, LA

ASCO Annual Meeting

For Roast Information
301.650.9127

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SuperGen, Inc.
US Oncology

Matrix Pharmaceutical Inc.
Medtronic Neurological
New Jersey Cancer Institute
Novartis Oncology
Varian Medical Systems

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THE CANCER LETTER

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Business & Regulatory Report

Formerly "Cancer Economics"

Oncology Management:

Cytogen Corp.'s Imaging Agent ProstaScint Added To NCCN Prostate Cancer Guidelines

Cytogen Corp. (Nasdaq: CYTO) of Princeton, NJ, said the **National Comprehensive Cancer Network,** an alliance of academic cancer centers, has added the Cytogen imaging agent, ProstaScint, to its Practice Guidelines for Prostate Cancer.

ProstaScint identifies the extent of prostate cancer in newly diagnosed patients at high risk for metastatic spread and with recurrent prostate cancer, the company said. ProstaScint employs a monoclonal antibody linked to a radioactive isotope and directed to prostate specific

(Continued to page 2)

Product Approvals & Applications:

FDA Grants Six-Month Priority Review To Nolvadex For DCIS Adjuvant Treatment

AstraZeneca, of Stockholm, said the FDA has granted a six-month priority review to its breast cancer drug, Nolvadex (tamoxifen citrate), for the adjuvant treatment of ductal carcinoma in situ following surgery and radiation.

The company said there is currently no FDA-approved medication for the adjuvant treatment of DCIS, which accounts for nearly 20 per cent of all newly diagnosed breast cancer cases.

"If approved for this indication, Nolvadex's effectiveness will have been demonstrated across several stages of the breast cancer continuum from risk reduction in women at high risk to advanced breast cancer," said Gerard Kennealey, vice president of Medical Oncology.

* * *

ALZA Corp. (NYSE: AZA) of Mountain View, CA, said FDA has approved its new drug application for Viadur, a once-yearly leuprolide acetate implant for the palliative treatment of advanced prostate cancer.

Viadur, developed by ALZA on behalf of **Crescendo Pharmaceuticals Corp**. (Nasdaq: CNDO) is a miniature titanium implant with an osmotic engine which delivers precise levels of leuprolide, the company said. ALZA said it has exercised its option to obtain a worldwide license for Viadur from Crescendo.

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Aphton (Nasdaq: APHT) of Miami said FDA has accepted its IND application for a combination immuno-chemo therapy regimen of anti-G17 immunogen and 5-FU plus cisplatin to begin late-stage clinical trials

(Continued to page 7)

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Prostate Cancer Guidelines Of NCCN Include ProstaScint

(Continued from page 1)

membrane antigen— PSMA, the Cytogen proprietary cancer marker, the company said.

"These guidelines are important to patients, because NCCN recommends ProstaScint be considered in the clinical evaluation of the majority of men who exhibit evidence of recurrent prostate cancer, and for selected patients with newly diagnosed disease," said Michael Manyak, professor and chairman, Department of Urology, George Washington Medical Center.

* * *

Endocare Inc. (Nasdaq: ENDO) of Irvine, CA, said Tricare, a managed healthcare program for active duty and retired members of the uniformed services, their families and survivors, will cover prostate cryosurgery procedure, Endocare said. There are 173 medical centers within the VA healthcare system serving an estimated 2.5 million patients annually.

* * *

Myriad Genetics Inc. (Nasdaq: MYGN) of Salt Lake City, said it has exclusively licensed **MDS Laboratory Services**, of Toronto, to offer the BRACAnalysis molecular diagnostic test to Canadian women who are at risk of breast and ovarian cancer.

Under the agreement, MDS said it will send test requests for the BRACAnalysis test to Myriad for analysis, and will establish a service in Canada to provide individual mutation screening tests. Myriad said it intends to explore opportunities for additional testing services and other ways to expand its relationship with MDS.

The agreement represents a strategy to expand the Myriad molecular diagnostics business into multiple foreign markets during 2000, the company said. The company said it had recently launch testing services in Japan, the UK and Ireland. Myriad said it plans to further increase the domestic market penetration of its existing molecular diagnostic tests in addition to continued development of foreign markets.

* * *

US Oncology Inc. (Nasdaq: USON) of Houston said it earned $68.4 million ($0.67 per share) on revenues of $1.093 billion for the year ended Dec. 31, 1999. Last year, the company's earnings were $60 million ($0.60 per share), and revenues $836.6 million.

The results do not include costs associated with the merger of Physician Reliance Network and American Oncology Resources.

During the fourth quarter of 1999, the company said it decided to sell approximately 1.26 million shares of Ilex Common Stock resulting in net after tax proceeds of $39.1 million in the first quarter of 2000.

As a result of the sale, the company said it recognized a net income of $9 million ($0.09 per diluted share) for the fourth quarter of 1999 and will recognize $17.2 million ($0.17 per diluted share) in the first quarter of 2000.

The company also said its board of directors has authorized the repurchase of up to 10 million of its common shares in public or private transactions. This figure represents 9.9% of the total shares issued and to be issued at December 1999.

"The company made a strategic decision in the fourth quarter of 1999 to sell its Ilex stock in order to invest in a stock repurchase program," R. Dale Ross, chairman and CEO, U.S. Oncology said in a statement.

"The post-merger integration process required substantial resources and consolidation," Ross said. "Our management and physician leadership made considerable progress in the integration of our financial reporting, clinical research programs and information systems."

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Deals & Collaborations:

Bristol-Myers, Karolinska In Collaboration For Studies

Bristol-Myers Squibb Co. (NYSE: BMY) of Princeton, NJ and the **Karolinska Institute** of Stockholm said they have entered into a three-year collaboration to integrate pharmacogenomics with clinical trial programs in cancer.

"We intend to expand this initiative to include other major clinical trial centers, as well as to ultimately apply pharmacogenomics across all of our therapeutic areas," said Peter Ringrose, president, BMS Pharmaceutical Research Institute. "Pharmacogenomics is the key to personalized medicine. We believe it will revolutionize the treatment of many diseases, from cancer to cardiovascular disease to central nervous system disorders to infectious diseases."

* * *

Celera Genomics (NYSE: CRA) of Rockville, MD, and **City of Hope Cancer Center**, of Duarte, CA, announced a collaboration to investigate associations of genetic polymorphisms with breast cancer. The collaboration combines City of Hope's clinical genetics approach with the Celera DNA sequence information and polymorphism information databases.

Celera said it would retain the rights to all information generated from the collaboration in its database products. All intellectual property developed through this collaboration will be jointly owned by Celera and City of Hope, the companies said.

"This research collaboration with City of Hope should add significant value to our polymorphism information," said Sam Broder, chief medical officer of Celera and former director of NCI. "We hope that this collaboration will enable clinical investigators to develop better ways to prevent, diagnose, and treat breast cancer."

* * *

EDAP TMS S.A. (Nasdaq: EDAYE and EASDAQ: EDAP) of Vaulx-en-Velin, France, said it has reached a new research and development agreement with SIEMENS AG for the development of the EDAP proprietary High Intensity Focused Ultrasound technology for breast cancer treatment. SIEMENS will fund 50 percent of the costs of the new program, the company said.

Under the agreement, EDAP TMS and SIEMENS will jointly develop a research program and clinical trials, with the support of Heidelberg and Iena Universities, to treat breast tumors, using magnetic resonance imaging visualization and the HIFU technology.

* * *

Elan Corp. plc (NYSE: ELN) of Dublin and **The Liposome Co. Inc.** (Nasdaq: LIPO) of Princeton, NJ, said they have entered into a merger agreement under which Elan will acquire Liposome.

Liposome will operate as a separate business unit within Elan, the company said.

Under the terms of the agreement, Elan will acquire all of Liposome's outstanding stock in a tax-free, stock-for-stock transaction, the company said.

The transaction is expected to close later this year, the company said.

* * *

Genzyme Molecular Oncology (Nasdaq: GZMO) of Framingham, MA, said it has exclusively licensed dendritic/cancer cell fusion technology for all therapeutic uses from **Dana- Farber Cancer Institute**.

The company said it is funding a phase I breast cancer vaccine trial, using the cell fusion technology, at the Beth Israel Deaconess Medical Center, a member of the Dana-Farber/Harvard Cancer Center.

The trial will enroll patients with late stage metastatic breast cancer and should be completed in 2000.

David Avigan, clinical director of the bone marrow program at BIDMAC and principal investigator of the trial, said he has received FDA clearance to study the technology in melanoma patients. Studies in kidney cancer are also being planned. Genzyme said it would fund the trials through the Dana-Farber/Harvard Cancer Center.

* * *

Human Genome Sciences Inc. (Nasdaq: HGSI) of Rockville, MD, **Vical Inc**. (Nasdaq: VICL) of San Diego, and **Vascular Genetics Inc.** of Research Triangle Park, NC, said they have agreed to develop novel genes as pharmaceutical products to treat or prevent a number of diseases.

The products would use the Vical patented naked DNA delivery technology and novel genes within the HGS proprietary database, with initial product development at VGI, the companies said.

Vical and HGS said they have signed a reciprocal royalty-bearing license. Under the agreement, Vical has the option to exclusively license up to three genes from the HGS proprietary genomics database for

gene-based product development. HGS has the option to license the Vical patented naked DNA gene delivery technology for use in up to three gene-based products, the companies said.

Vical said it is granting an exclusive, royalty-bearing license to VGI for naked DNA delivery of Vascular Endothelial Growth Factor-2 (VEGF-2). VGI, a privately held company in which HGS is a major shareholder, has initiated clinical trials using naked DNA delivery of the VEGF-2 gene to promote angiogenesis with coronary artery disease and critical limb ischemia. In exchange, Vical will receive a minority equity interest in VGI, the companies said.

* * *

ILEX Oncology Services Inc. of San Antonio said it has acquired the U.S.operations of **British Biotech plc** (Nasdaq: BBIOY) of Oxford, UK.

As the new owner of the Annapolis, MD facility, ILEX said it would provide ongoing clinical development of marimastat for British Biotech in North America. Marimastat is currently being investigated in seven phase III studies for a range of solid tumors, the company said.

"In addition to an important series of contracted projects and an already established workforce, this acquisition will allow us to interact more effectively with our East Coast-based customers," said Michael Dwyer, president of ILEX Oncology Services.

Clinical Trials:

Antigenics Begins Phase II Trial Of Oncophage For NHL

Antigenics Inc. (Nasdaq: AGEN) of New York, NY, said it has initiated a phase II trial of Oncophage for non-Hodgkin's lymphoma.

"We are encouraged by the preliminary results from other clinical trials with Oncophage," said Anas Younes, lead trial investigator at M.D Anderson. "Lymphoma has been shown to respond to cancer immune therapies; the non-toxic nature of this protein-based product is a wonderful added benefit to this treatment."

"The genomics field has begun to confirm what we have known from immunological studies for several decades—that each patient's cancer contains a unique profile of antigenic signals that must be addressed by a personalized treatment," said Garo Armen, chairman and CEO of Antigenics.

* * *

AVAX Technologies Inc. (Nasdaq: AVXT) of Kansas City, MO, said it has initiated a multi-center phase II study of M-Vax, its autologous therapeutic cancer vaccine for patients with stage IV melanoma who have measurable disease, but limited primarily to lung metastases.

The patients will receive seven weekly M-Vax vaccinations followed by a six-month booster, the company said. The study seeks to evaluate the M-Vax ability to cause tumor regression in patients with more advanced disease. AVAX said it is conducting a registration trial of M-Vax in stage III melanoma.

The phase II trial is the result of promising data gathered from 16 stage IV melanoma patients with lung metastases, which suggested that treatment with M-Vax may result in lung tumor regression, the company said. The data indicated that tumor regression was observed in four of the 16 patients, with three ranging from 75 to 90 percent shrinkage and a fourth showing just under 50 percent shrinkage. The four patients whose tumors shrank also experienced survival beyond normal expectations, which is usually considered to be 6-12 months after being diagnosed with stage IV melanoma, the company said.

"Clinical studies of M-Vax continue to demonstrate M-Vax's potential to provide long-term therapeutic benefit to patients that have been diagnosed with later stage melanoma, including those with metastases to the lung," said Jeffrey Jonas, president and CEO of AVAX Technologies.

* * *

BSD Medical Corp. (OTC: BSDM) of Salt Lake City said **Duke University** has joined the European Oncology and Radiation Therapy Committee for phase III clinical trials using the BSD-2000 regional deep hyperthermia system for soft tissue sarcoma.

The 10 clinical trials in the U.S. and Europe using BS-2000 combine hyperthermia and chemotherapy to eliminate amputation, the company said.

The company said phase II trails conducted at the Department of Medical Oncology of Klinikum Grosshaden of Munich LMU University have shown that hyperthermia, using the BSD-2000 system, provides a supra-additive effect on several chemotherapeutic agents, increases disease-free survival time and eliminates amputation for some patients, the company said.

The study patients were non-responders with a life expectancy of a few months—their only option was radical amputation. After hyperthermia

treatment, 87% were able to have their tumors resected without amputation or removal of normal tissue structures, and 47% were alive and free of disease after four years. As an independent effort, Duke University has used the BSD-2000 to conduct phase II trials combining hyperthermia and radiation treatments achieving excellent local control, particularly for extremity soft sarcomas, with a 10-year actuarial local control of 94% for that group, the company said.

In a related development, BSD Medical Corp. said it had submitted to FDA the Duke University clinical study using hyperthermia to release liposome-encapsulated doxorubicin for ovarian cancer treatment.

* * *

Cell Pathways Inc. (Nasdaq:CLPA) of Horsham, PA, said it has completed enrollment in an open-label phase II study of Aptosyn, a treatment for precancerous colon polyps in children with familial adenomatous polyposis.

The study will investigate whether Aptosyn, a selective apoptotic anti-neoplastic drug which inhibita cyclic GMP phosphodiesterase and selectively induces in abnormally growing precancerous and cancerous cells, reduces the number of polyps after one year of treatment, the company said. All participants receive a baseline colonoscopy at enrollment, and a second colonoscopy following one year of therapy with Aptosyn. Following the one-year trial, all participants are eligible to continue on treatment as part of extension studies.

"After obtaining initial safety data from a small number of pediatric patients, we expanded enrollment in this study to include a total of twenty children with FAP, each of whom has colon polyps," said Rifat Pamukcu, chief scientific officer and senior vice president of research and development at Cell Pathways. "Normally, these patients require surgical removal of most of their colon as teenagers or young adults to reduce their risk of colon cancer. We hope to see a stabilization in polyp formation followed by a reduction in the number of polyps in these young patients, with the subsequent goal of preventing or delaying the need for surgery. We are also considering additional clinical trials in this pediatric population," Pamukcu said.

* * *

Digene Corp. (Nasdaq: DIGE) of Gaithersburg, MD, said preliminary results of the NCI Ascus/Lsil Triage Study, and Alternatives in Women's Health Care trial indicate that the Digene HPV Test is 96% sensitive in detecting cervical disease in women with ASCUS Pap smear diagnoses while the expert Pap smear used in the trial was 85% sensitive.

"Based on these conclusive results, HPV testing should become the method of choice for patient management of women with ASCUS Pap smear results," said Evan Jones, chairman and CEO of Digene Corp. "Doctors have struggled to tell the difference between women whose borderline abnormalities will go away without treatment and those that will progress to a precancerous condition or cancer. We now have data from the largest study in the field that the Digene HPV Test can determine definitively those women who are at risk for the development of cervical cancer. The ALTS results could affect positively the management of the approximately 3 million women each year who have borderline Pap smear results," Jones said.

* * *

IBC Pharmaceuticals, LLC, a joint venture between **Immunomedics Inc.** (Nasdaq: IMMU) of Morris Plains, NJ and **Beckman Coulter Corp.** (NYSE: BEC) of Fullerton, CA, said it has begun phase I/II clinical trials of Pentacea for the treatment of solid tumors. The clinical trial is open at two sites in France.

"Pentacea delivers cytotoxic radiation directly to tumors that express carcinoembryonic antigen. CEA is expressed on most major solid tumors including those of the breast, colon, and lung," said John Reno, executive vice president of IBC Pharmaceuticals.

At the outset of Pentacea treatment, a bispecific antibody is administered to a patient. One part of the bispecific antibody targets the tumor and the other part will bind to the subsequently administered radioactive small molecule. Upon administration, the radioactive small molecule binds to the bispecific antibody at the tumor. Any unbound radioactivity is rapidly eliminated from the body through the kidneys, the company said.

"Using this technology, the toxicity normally observed with directly radiolabeled antibodies should be reduced thus permitting larger doses of radiation to be administered with improved therapeutic potential," Reno said.

* * *

ImClone Systems Inc. (Nasdaq: IMCL) of New York, NY, said it has been awarded a phase I small business innovation research grant by NCI to study the effect of active immunization on the

inhibition of tumor angiogenesis.

ImClone said the study will seek to stimulate the immune system to target Flk-1, a key receptor in blood vessel formation, which binds to vascular endothelial growth factor (VEGF). The objective will be to demonstrate the feasibility of developing a vaccine against tumor blood vessels for the safe and efficacious treatment of cancer, the company said.

"The VEGF receptor is an exciting area of research in cancer therapy, potentially offering multiple approaches to the development of new therapeutics," stated Harlan Waksal, executive vice president and CEO of ImClone. "ImClone's research teams have extensive experience in the role of VEGFr in angiogenesis, as well as expertise in cancer vaccines. This new, SBIR-supported program brings these disciplines together, allowing us to further explore the inhibition of VEGFr through immune activation."

* * *

Immune Response Corp. (Nasdaq: IMNR) of Carlsbad, CA, said it has begun a phase I trial with the **Cedars-Sinai Medical Center** Maxine Dunitz Neurosurgical Institute of a vaccine for malignant brain tumors.

The vaccine is designed to induce the immune system to recognize and destroy tumor cells, thereby preventing or delaying the recurrence of malignant brain tumors such as glioblastoma multiforme and anaplastic astrocytoma, the company said.

"Rather than bombarding the patient with chemicals and radiation, we're devising strategies that interfere with the cancer cells' very existence," said Keith Black, neurosurgeon and principal investigator of the trial at Cedars-Sinai. "The vaccine approach is part of a new generation of potential therapies based on the latest biologic information about how brain tumors survive and what allows them to grow."

* * *

Incyte Genomics Inc. (Nasdaq: INCY) of Palo Alto, CA, will be the new formal corporate name for **Incyte Pharmaceuticals Inc.**, effective later this year pending stockholder approval, the company said.

"The Incyte name has become synonymous with innovation in genomics research," said Roy Whitfield, Incyte CEO. "Incyte Genomics builds on the power of our existing market position and more accurately reflects the role we play in advancing greater and more meaningful understanding of the molecular basis of disease."

"The name Incyte Genomics communicates that we are committed to revolutionizing health care through the discovery and application of genomic information and technology," said Randy Scott, president and chief scientific officer of Incyte. "We are also as deeply committed to making this genomic information broadly available on a non-exclusive basis to pharmaceutical, biotechnology, and academic researchers all over the world."

Incyte Genomics said it would offer all of its products online by the end of this year and will begin the first phase of LifeSeq GENE-BY-GENE, its e-commerce genomics program. The new offering will give researchers affordable access to its collection of gene sequence data or physical copies of genes, one gene at a time, the company said.

* * *

Matrix Pharmaceutical Inc. (NNM: MATX) of Fremont, CA, said it has initiated two clinical trials using its anti-cancer coumpound, FMdC, to study it in combination with other chemotherapeutic agents.

"Combination cancer chemotherapy has become the norm in clinical practice," said Michael Casey, chairman and CEO of Matrix. "Our pre-clinical studies show that FMdC is synergistic in combination with other chemotherapies. The results of these two trials will be important in determining our future development path for FMdC."

"Cisplatin has proven to be one of the most broadly effective anti-cancer agents available to physicians and has had particular value in combination with other agents that have complementary or synergistic mechanisms of action and non-overlapping toxicities," said Richard Leavitt, senior vice president of Medical and Regulatory Affairs for Matrix. "The data for FMdC lead us to believe that FMdC combined with cisplatin could enhance the anti-cancer activity of both agents."

The company said it had begun a phase I dose escalation trial with FMdC in combination with 5-FU (fluorouracil) at Dana Farber Cancer Center.

* * *

Regeneron Pharmaceuticals Inc. (NASDAQ: REGN) of Tarrytown, NY, and **Medarex Inc**. (NASDAQ: MEDX) of Princeton, NJ, announced a collaboration to develop and commercialize human antibodies as therapeutics.

Regeneron said it will contribute its expertise in proteins as drug discovery targets, and Medarex said it would contribute its HuMAb-Mouse technology to create fully human antibody products for those targets. The companies said they have selected more

than 20 initial targets, including growth factors, cytokines, and receptors.

In the binding memorandum of understanding, Medarex and Regeneron said they agree to share preclinical and clinical responsibilities, and to jointly market any drugs that result from the collaboration.

* * *

Vion Pharmaceuticals Inc. (Nasdaq: VION) of New Haven, CT, said it has received approval for a phase I trial of its bacterial vector, Tapet, and said it has signed a letter of intent for a five-year cooperative research and development agreement with NCI.

The phase I trial seeks to answer the following: to determine the safety and tolerability of intravenously injected Tapet in patients with advanced cancer and Tapet's ability to penetrate and preferentially replicate within tumor metastases, the company said. Both clinical and subsequent preclinical studies will be under the direction of Steven Rosenberg, chief of Surgery, Division of Clinical Sciences, NCI, cancer researcher and authority on the application of cytokines, tumor vaccines and other biologicals in cancer patients, the company said.

Under the terms of the CRADA, Vion said its scientists will provide a variety of Tapet vectors for further evaluation. Rosenberg will evaluate VNP20009 in additional murine models and in combination with other anticancer agents, and explore the mechanisms by which the bacterial vectors cause antitumor activity. The company said the CRADA would enable future preclinical studies of second generation armed Tapet vectors (bioengineered to express certain potent anticancer agents) and clinical trials that are predicated on the antitumor activity demonstrated in mouse models.

Product Approvals & Applications:

Aphton To Test Anti-Gastrin Drug At M.D. Anderson

(Continued from page 1)

for metastatic stomach cancer.

As a preliminary to the large scale, randomized, double-blind, multi-centered trial, a small number of patients will be immunized to determine immune responsiveness of the regimen to be used. The primary center for the trials will be M.D. Anderson Cancer Center with patient recruitment to begin in April.

Aphton said its anti-gastrin drug induces a directed antibody response against gastrin and other gastrin-related growth factors. Gastrin has been established as a central hormonal growth factor that stimulates gastric cancer cells to proliferate and spread, the company said.

* * *

BioChem Pharma Inc. (Nasdaq: BCHE; TSE: BCH) of Laval, Quebec, Canada, said the FDA has approved PACIS BCG, Live, its immunotherapy against bladder cancer, for sale in the U.S. The drug will be distributed in the U.S. by **UroCor Inc.** (NASDAQ: UCOR), of Oklahoma City, the company said.

BioChem said it will continue to manufacture the drug in its Quebec- based facilities. Approved for use in several other countries, including Canada, the product features the Armand-Frappier strain of Bacillus Calmette-Guerin, which has been in clinical use for a number of years worldwide, the company said.

* * *

BioNumerik Pharmaceuticals Inc. of San Antonio said FDA has granted Fast Track designation for the development of its BNP7787 to prevent or decrease the nerve damage associated with paclitaxel.

BNP7787 could protect against common toxicities of radiation therapy and is currently undergoing phase 1 trials at the University of Chicago, Roswell Park Cancer Center in the U.S. and at the Free University Hospital in Europe, the company said.

Paclitaxel induced nerve damage can be severe enough to cause patients and physicians to stop cancer treatment, thereby limiting the amount of the drug that can be given to control the growth of cancer. Currently, there is no approved drug that is safe and effective in protecting against paclitaxel induced nerve damage, the company said.

"One of the objectives of the ongoing phase I trials is to evaluate the frequency and severity of chemotherapy associated nerve damage in cancer patients receiving BNP7787 who are given standard chemotherapy drugs that are known to have common toxic side effects, including nerve damage, said Frederick Hausheer, chairman and CEO of BioNumerik. "In these phase I trials we have observed a substantial reduction in the frequency of patients with chemotherapy induced nerve damage compared to the expected incidence of nerve damage in patients who were treated with the same chemotherapy drugs without BNP7787. The severity of the chemotherapy induced nerve damage is greatly

reduced from what would otherwise be expected to occur in similarly treated patients. We have observed that BNP7787 appears to have a high degree of safety in cancer patients — clinically important side effects from BNP7787 have not been observed, even when the drug is administered at high doses" Hausheer said.

"BNP7787 is well tolerated by patients and does not complicate administration of chemotherapy. We are encouraged that few patients have had clinically significant nerve damage and that anti-tumor responses have been seen," said Richard Schilsky, associate dean for clinical research at the University of Chicago and principal investigator for the BNP7787 phase I trial.

* * *

Cell Therapeutics Inc. (Nasdaq:CTIC) of Seattle, said its cancer drug treatment, Arsenic Trioxide, was granted Fast Track designation by FDA for acute promyelocytic leukemia.

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Interpore Cross International (Nasdaq:BONZ) of Irvine, CA, said it has received a humanitarian device exemption from FDA to market its Telescopic Plate Spacer, an expandable titanium implant which replaces vertebral bodies removed due to cancer.

Metastatic spinal tumors are most often located in a vertebral body, and the corpectomies performed to remove the tumors result in destabilization of the spine, the company said.

* * *

Introgen Therapeutics Inc.of Austin, TX, said the NIH Recombinant DNA Advisory Committee completed a review of its phase III gene therapy clinical study for head and neck cancer.

The NIH RAC did not recommend that the sponsors, Introgen Therapeutics and Aventis Pharmaceuticals, make any changes to the phase III trial design. The trials will be conducted at 60 centers in the U.S., Canada and Europe.

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SciClone Pharmaceuticals (Nasdaq: SCLN) of San Mateo, CA, said FDA has granted orphan drug status to its immunotherapy drug, Zadaxin, for hepatocellular carcinoma.

SciClone said its phase II liver cancer trials will begin later this year and will be based on the same protocols as a previous study in Italy combining Zadaxin immunotherapy with TACE. In that pilot study, the combination resulted in a statistically significant increase in survival compared to a matched historical group receiving TACE alone. Patients receiving the combination also showed an increase in peripheral blood immune cells, which are fundamental in the destruction of cancer cells. No additional side effects were observed from the addition of Zadaxin, the company said.

NAS RFP: Intellectual Property

Request for Proposals: National Academies Board on Science, Technology, and Economic Policy Research on Intellectual Property in the Knowledge-Based Economy

The Science, Technology, and Economic Policy board is undertaking a study of intellectual property policy to address the following questions: What are the consequences of the series of legislative actions, judicial decisions, institutional changes, and international agreements that have marked IP policy over the past 20 years? What benefits have been derived? What problems may be emerging? Are there respects in which the extension of IPRs should proceed further to encourage technical advance, investment, and innovation or, in view of claims that in some circumstances IPRs may be inhibiting competition and discouraging research and its communication and use, are there respects in which the extension of IPRs has proceeded too far?

Topics include Patent Administration and Litigation and Software-enabled Business Method Patents and Biotechnology Patents.

The projects should be policy-oriented and should be completed in 10-12 months. The board will consider proposals for analytical papers with budgets in the range of $5,000-7,000 and proposals for empirical research and data analysis in the range of $15,000 to $30,000. The project is chaired by Richard Levin, president, Yale University, and Mark Myers, senior vice president (ret.), Xerox Corporation.

The board requests submission to the email address below, preferably in Word format, of 2-5 page statements of interest by May 1. These statements should include a description of the proposed analysis or research, a description of the proposed methodology, and a brief statement of qualifications and related work. A statement need not address all of the questions listed under the general topic heading. The statements will be reviewed by a group of STEP members and advisers. Authors of proposals of interest will be contacted by May 15 for further discussion. Final selection will be made by June 1, 2000.

Inquiries: Stephen Merrill, executive director, board phase on Science, Technology, and Economic Policy, 2101 Constitution Avenue, N.W., FO-2014, Wash., DC 20418, phone 202-334-2200; fax 202-334-1505; e-mail Smerrill@nas.edu; To Submit Proposal Statements: STEP@nas.edu. Additional information is available at: www4.nas.edu/pd/step.nsf.

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