THE CANCER LETTER INTERACTIVE

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NCI Awards $59M Contract For Key Project To Consolidate Phase III Trial Administration

NCI has awarded a $59 million contract to Westat Corp. of Rockville, MD, to establish the Cancer Trials Support Unit, one of three pilot projects the Institute and its advisory groups developed last year in an attempt to restructure the national system of cancer clinical trials.

The CTSU will consolidate some of the expensive and redundant administrative tasks that the NCI-supported Clinical Trials Cooperative Groups perform, NCI officials said. These tasks include auditing group member institutions, credentialing investigators, and managing protocol

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In Brief:

NCI Registers Web Domain CANCER.GOV, Plans To Improve External Communications

CANCER.GOV: As part of a "branding" campaign, NCI has registered the domain name http://www.cancer.gov, which is easier on the acronym-challenged than www.nci.nih.gov. Also, the Institute hired a consultant in "metatags," the identifiers that Web search engines use to direct searchers to websites, in order to make it easier for people to find the Institute online, NCI Director **Richard Klausner** said to the Director's Consumer Liaison Group at its Oct. 18 meeting. However, the Institute's efforts to improve its website and tailor information to users is running into government privacy regulations and Paperwork Reduction Act regulations regarding surveys. NCI is seeking guidance from the Office of General Counsel, Klausner said. . . . **COMMUNICATION** will be an important issue for NCI over the next year, Klausner said to the DCLG. "We will quite dramatically ramp up and change the centrality of communication in this Institute, both from the viewpoint of research to the products, and a new and strengthening alliance with those to whom we communicate," Klausner said. "Instead of thinking of communications as an add-on to research, we are now articulating communications as part of our research agenda." Plans involve redesigning NCI's website, re-evaluating the Institute's communications structure, and a general "branding" campaign, Klausner said. NCI also is reviewing a list of recommendations the DCLG submitted earlier this year on improving the Institute's communications. **Barbara Rimer**, director of the NCI Division of Cancer Control and Population Sciences, is serving as chairman of the Extraordinary Opportunities in Communication Task Force. . . . **"THE**

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Westat, Groups Coalition, Oracle, Win NCI Contract

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approvals by Institutional Review Boards.

The CTSU also will function as a protocol support center. The unit is expected to provide World Wide Web-based patient registration, eligibility assessment, and data reporting for a specified "menu" of trials. Initially, the CTSU will support new phase III trials in breast, lung, genitourinary, and gastrointestinal cancers, and adult leukemia.

The concept for the CTSU grew out of a two-year effort by NCI, its advisory boards, and cooperative group chairmen to study the clinical trials system and develop methods for broadening physician and patient access to trials and completing studies faster.

In 1977, an NCI advisory group, chaired by James Armitage of the University of Nebraska Medical Center, made nearly four dozen recommendations for improving the clinical trials system, including increased funding to the cooperative groups, uniform data collection standards, and improved informatics systems (**The Cancer Letter**, Oct. 3, 1997).

A second panel, the Clinical Trials Implementation Committee, deliberated for nine months about specific ways to improve the system, without damaging it. (**The Cancer Letter**, Oct. 9 and June 12, 1998).

The CTSU was one of three pilot projects the Implementation Committee recommended. The committee also recommended that NCI form disease-specific concept review committees for the independent review of phase III studies, and hold "state-of-the-science" meetings with investigators to identify new research opportunities.

Goal To Reduce Administrative Burden

The CTSU could streamline clinical trials for the cooperative groups, physicians, and cancer patients, said Jeff Abrams, senior investigator in the NCI Cancer Therapy Evaluation Program.

For the eight cooperative groups that study adult cancers, the CTSU will reduce administrative burdens in regulatory affairs and auditing. Currently, if a hospital has physicians belonging to more than one cooperative group, each group must audit the hospital every three years. "Our hope is that over time, we will be able to do one single audit every three years for each institution," Abrams said to **The Cancer Letter**.

For investigators affiliated with the cooperative groups, the CTSU will provide an "open menu" of phase III trials, so that investigators will be able to enroll patients on any cooperative group trial the CTSU supports. Currently, investigators are limited in their ability to enroll patients on the studies of the groups to which they don't belong. The CTSU also will include educational components for physicians and clinical research associates.

For physicians who are not affiliated with cooperative groups, the CTSU eventually will enable them to participate more easily in clinical trials. This function of the CTSU is not expected to be fully operational for about two years, Abrams said. A protocol access and referral system will provide information on protocols, how to enroll and randomize patients, and how to send in data, Abrams said.

For cancer patients, the CTSU will link with NCI's PDQ database for information about clinical trials and cancer treatment, as well as specific insurance coverage. "The goal is to enable patients to find physicians who are participating in their area and who participate in their insurance plan," Abrams said. "We don't want to send people to physicians only for them to find they can't get on trials because of their insurance."

The CTSU will reimburse physicians directly for their research costs, and will provide "leadership"

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

Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 Fax: 202-362-1681
PO Box 9905, Washington DC 20016
E-mail: kirsten@cancerletter.com or paul@cancerletter.com

Customer Service: 800-513-7042
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funding to each trial's principal investigator and statistical office when a phase III trial is approved, Abrams said. Getting the funding out faster could help speed the start of new trials, he said.

Subcontracts To Groups Coalition, Oracle

Through a subcontract with Westat, the Coalition of National Cancer Cooperative Groups Inc., based in Philadelphia, will be responsible for the regulatory aspects of the program including auditing functions, other regulatory affairs, education, fiscal management, interacting with investigators, said Robert Comis, president of the coalition.

Support for systems development will be provided by Oracle Corp., of Redwood City, CA.

"The coalition is thrilled to be partners with Westat and Oracle in helping develop the CTSU for the NCI," Comis said. "What it does is provide a tremendous amount of experience from the perspective of Westat, a venerable contractor, the experience in the cooperative group structures and the tremendous power of Oracle.

"Most importantly, we are all committed to this being a real advance in making clinical trials more accessible first and foremost to the patients, but also to the physician investigators," Comis said. "Of all the innovations that have been suggested in the past few years, decreasing the redundancy in the system is something we've all seen the value of."

Comis said that even if the pilot project is successful and is expanded, it will not threaten the future of the cooperative groups. "NCI has made it absolutely clear that it values the groups and the group functions," he said. "We've been assured by everyone that the intention is not to compromise the groups, but to make group studies more available and accessible throughout the field, to our own investigators and to those who aren't engaged at the present time.

"The programs of the groups will still be the major engines for cancer clinical trials research," Comis said.

Further information about the clinical trials system restructuring is available at http://ctep.info.nih.gov (under "clinical trials support initiatives").

NCI published a booklet, "Clinical Trials, A Blueprint for the Future," describing the initiatives. The booklet is available by calling 800-4-CANCER or by email request to Jana Johnston at johnstoj@occ.nci.nih.gov.

In Congress:

Conferees Approve $2 Billion Budget Increase For NIH

A spending bill approved by House-Senate conferees gives NIH $17.613 billion, a $2 billion increase over last year.

The bill approved by the Appropriations Conference Committee on Labor, HHS and Education on Oct. 27 chose the Senate's funding level for NIH, giving the Institutes a 12.8 percent increase. The House bill provided a 9.2 percent boost for NIH.

Under the conference bill, NCI will receive $3.287 billion, a $384.5 million (13.2 percent) increase.

In a departure from established procedure, the Labor, HHS bill went to conference before being approved by the full House. The Republican plan is to combine the spending bills for Labor, HHS and Education and the District of Columbia, Capitol Hill sources said. The D.C. bill was recently vetoed by the President.

In floor remarks, Sen. Arlen Specter (R-PA), chairman of Labor, HHS and Education Subcommittee of the Senate Appropriations Committee, said the combined bill is likely to be vetoed by the President.

The issues in dispute do not involve NIH funding. In the Labor, HHS bill, Congress and the President are clashing over plans to provide additional money for school districts. In the D.C. bill, the dispute involves Congressional language that precludes the use of public and private funds for needle exchange. However, the Republican position was recently watered down to preclude only the use of public funds for this purpose.

Obituaries:

Eleanor Nealon, 59, NCI Liaison To Cancer Patients, Advocates

Eleanor Nealon, director of the NCI Office of Liaison Activities, died at her home in Bethesda, MD, on Oct. 22. She was 59. The cause of death was metastatic breast cancer.

Nealon became an important voice for cancer patient advocacy within NCI as the first director of the liaison office, which was established in 1994. Nealon created a new model for interaction between a government agency and consumers with the formation of the NCI Director's Consumer Liaison Group in 1997. Working with advocates, Nealon

devised a process for selecting consumers to serve on this panel, which advises the NCI director on issues of importance to consumers and works to communicate information about NCI activities to consumer organizations.

Last year, Nealon received awards for her work from the National Coalition for Cancer Survivorship and the Cancer Research Foundation of America.

NCI has established the Eleanor Nealon Extraordinary Communicator Lecture Series to honor Nealon's memory, Institute Director Richard Klausner announced at a meeting of the DCLG on Oct. 18.

"I am honored to establish this lecture series in Eleanor's name, because she cared so deeply about cancer survivors' needs and concerns, rights and views; and sparked the creation of an office for NCI that became a bridge for communication and collaboration between the Institute and the community of cancer survivors," Klausner said. "Her office later became a model for the rest of the NIH."

NCI plans to invite leaders in communications from academia, the media, business, and government to speak at the Institute, Klausner said. Improving cancer communications is one of the Institute's priorities, or "extraordinary opportunities," in its FY2001 Bypass Budget.

Nealon was born in Washington, DC, and attended Rosemont College, in Rosemont, PA. The college later awarded her an honorary Doctor of Literature degree. From 1971 to 1977, she worked as a medical writer and then director of public relations at Georgetown University Medical Center. She joined NCI in 1981 as a science writer.

In her career, she wrote numerous articles and educational materials. Over 1 million copies of her booklet for cancer patients, "What are Clinical Trials All About?" have been distributed.

Nealon was a member of the National Association of Science Writers, the American News Women's Club, and served on the advisory boards of the NIH Women's Health Initiative, the American Society of Hospital Public Relations, and the American Society of Clinical Oncology.

Nealon is survived by her husband, Anthony Wolbarst; her mother, Eleanor Nealon; a sister, Kathleen Nealon Detgen; two brothers, Stephen and Kevin, and nine nieces and nephews.

Memorial contributions may be made to Lombardi Cancer Center, New Research Building, Suite 501, 3970 Reservoir Rd. NW, Washington, DC 20007.

Benno Schmidt, 86, Advocate For National Cancer Program

Benno Schmidt, 86, a pioneering venture capitalist and one of the architects the National Cancer Program, died of heart failure Oct. 21.

As a member of the National Panel of Consultants established in 1970 by Sen. Ralph Yarborough, Schmidt helped shape the National Cancer Act of 1971. On the panel, Schmidt advocated giving the cancer program a unique, high-priority status within the government-financed biomedical research enterprise.

After the passage of the Act, Schmidt was named chairman of the President's Cancer Panel. In that role, he helped NCI secure its first substantial appropriation: $100 million in 1972. Two years later, in 1974, the panel met with then-President Richard Nixon and convinced him to support legislation to create the National Research Service Awards, for training biomedical scientists.

Schmidt's work, in association with John Hay Whitney, involved making investments in promising technologies. In fact, the two financiers are credited with coining the term "venture capital," by shortening the word "adventure," The New York Times reported.

Schmidt was the former chairman of the Memorial Sloan-Kettering Cancer Center Boards of Overseers and Managers. At the time of his death, he was the honorary co-chairman of the boards.

In a letter to MSK staff, cancer center President Paul Marks quoted a remark Schmidt made at an event marking the 15th anniversary of the passage of the National Cancer Act:

"I wish there were a faster way that we could cure disease without going through the laborious process of trying to understand it. Unfortunately, there are no shortcuts. In the most literal sense of the words: *life is not that simple.*"

Science Policy:

Ability To Interpret Atomic Vets' Death Rates Limited, IOM Finds

In the largest-ever study of the causes and rates of death among nearly 70,000 soldiers, sailors, airmen, and marines who participated during the 1950s in atmospheric nuclear tests, researchers have concluded that there is no difference between the atomic test participants and other military veterans in overall death rates or in total deaths from cancer.

The researchers at the Medical Follow-up Agency of the IOM looked at whether participants' death rates were higher than those of a comparison group of nearly 65,000 military personnel serving at the same time but not involved in the tests. They did not examine differences in nonfatal disease or injury.

The difficulties in doing such a retrospective epidemiologic study are manifold: Many years have passed since the tests, and the extent to which each serviceman was exposed is extraordinarily hard to determine because of the limited amount of exposure data collected at the time.

Participants in the nuclear tests had a 14 percent higher death rate from leukemia than those in the comparison group, but this difference is not statistically significant, the study said.

Because leukemia was originally singled out as a primary target for investigation, the researchers also looked at subcategories of participants. For example, land-based participants—those in the Nevada desert—had a death rate from leukemia that was 50 percent higher than military personnel in similar units who did not take part in atomic tests. Sea-based test participants in the South Pacific, however, did not differ from their comparison group in leukemia deaths.

The leukemia findings are consistent with those of other studies of atomic test participants, the study group said. The handful of other studies conducted have found slightly increased rates of leukemia.

The study report also points out some unanticipated results regarding two other kinds of cancer—prostate and nasal. Deaths from prostate cancer were 20 percent higher among test participants than the comparison group, and even higher for nasal cancer. The prostate cancer findings have not been consistently seen in other studies of people exposed to radiation and are therefore difficult to interpret. The nasal cancer finding is even harder to interpret, in part because this is the first study of atomic test participants to look specifically for that cause of death. To date, nasal cancer has not been among the cancers considered to be caused by radiation.

To improve understanding of the associations observed, researchers would need a crucial set of missing data—information on the size of the radiation dose received by each veteran. At the time of the tests, dose data were not being collected specifically for medical research; dose measurement and records maintenance was neither complete nor consistent. In the ensuing decades, the federal government has used the available information to reconstruct doses—not for research purposes, but to support veterans' claims for compensation. After a review of available data, the IOM did not use the dose information, finding it unsuitable for research of this kind.

This latest report supersedes an IOM report published in 1985. Several years after completion of the first study, substantial inaccuracies were discovered in the data provided to the researchers. The study was funded by the Defense Threat Reduction Agency of the Department of Defense.

Copies of "The Five Series Study: Mortality of Military Participants in U.S. Nuclear Weapons Tests" are available from the National Academy Press, phone 202-334-3313 or 800-624-6242.

NIH Programs:

The Mouse Is Next In Line For DNA Sequencing, NIH Says

The genetic makeup of the mouse, one of the most frequently used mammals in medical and behavioral research, will be deciphered in a research program begun this month by NIH.

Ten laboratories, called the Mouse Genome Sequencing Network, collectively will receive $21 million for the first seven months of funding. Mapping, which is determining the physical organization of the mouse's 21 chromosomes, and sequencing or identifying the order of the estimated three billion chemical bases, or letters, of the DNA in the mouse genome, are expected to be completed in working draft form in three years.

"Because mice and humans share many of the same fundamental biological and behavioral processes, this animal is one of the most significant laboratory models for human disease," said NIH Director Harold Varmus. "Knowing the genetic make-up of the mouse, and being able to compare it to the DNA of humans and other animal species, will greatly expedite many avenues of research including assessing predisposition to disease, predicting responses to environmental agents and drugs, and designing new medicines."

The Mouse Genome Sequencing Network is funded by every institute at NIH. Research on the mouse genome will occur in two stages, following the strategy being used by the international Human Genome Project to sequence the genetic blueprint of the human. Scientists working on the mouse genome first will complete an intermediate working draft

version of the animal's genetic instructions. This first stage will be completed no later than 2003. They then will turn their attention to filling gaps in the draft and finishing the sequence in final form by 2005.

"Many scientists have told us that sequence data, even in working draft form, is very useful to their research. For that reason, the Human Genome Project and now the mouse sequencing effort will complete their work in these two stages," said Francis Collins, director of the National Human Genome Research Institute of NIH.

By spring 2000, the Human Genome Project will produce a working draft of the genetic blueprint of the human. By 2003, or possibly sooner, the finished, high quality version of the human genome will be completed. One quarter of the human genome already has been sequenced by an international consortium of research centers including three laboratories supported by NHGRI. All of the sequence data is available to the public within 24 hours via Genbank (http://www.ncbi.nlm.nih.gov/Genbank).

"The success of the Human Genome Project, the recent advances in technology, and the broad support from the scientific community have allowed the NIH to take on sequencing the mouse genome," said Collins. "Prior to last year, this task was not officially one of our goals because several years ago it seemed too daunting to try to sequence both genomes."

This international sequencing effort has already deciphered the genomes of the bacterium E. coli, which has five million base pairs in its genetic blueprint; Baker's yeast, with 12 million base pairs; and the roundworm, C. elegans, with 97 million base pairs. The genome of the fruitfly, with 140 million base pairs, will be completed soon.

Recipients of the NIH grants and the principal investigators are:

—The Institute for Genomic Research, Rockville, MD; William Nierman

—University of Utah, Salt Lake City; Robert Weiss

—Washington University School of Medicine, St. Louis, MO; John McPherson

—Baylor College of Medicine, Houston, TX; Richard Gibbs

—NIH Intramural Sequencing Center, Gaithersburg, MD; Eric Green

—Albert Einstein College of Medicine, Bronx, NY; Raju Kucherlapati

—Whitehead Institute for Biomedical Research, Cambridge, MA; Eric Lander

—Cold Spring Harbor Laboratory, Cold Spring Harbor, NY; Richard McCombie

—Genome Therapeutics Corp., Waltham, MA; Douglas Smith

—University of Oklahoma, Norman; Bruce Roe.

Funding Opportunities:
Program Announcements

PAR 94-004: Cancer Education Program

The purpose of the R25 Cancer Education Grant Program is to provide continuing support for curriculum-driven programs that are directed at developing and sustaining innovative educational approaches that ultimately will have an impact on reducing cancer incidence, mortality and morbidity, as well as on improving the quality of life for cancer patients. These grants can focus on educational activities before, during and after completion of a doctoral level degree, as long as they address a need that is not fulfilled adequately by any other grant mechanism available at NIH, and are dedicated to areas of particular concern to NCI.

The CEGP, which can provide support to institutions for up to 5years, can focus on education activities before, during and after the completion of a doctoral level degree as long as they address a need that is not fulfilled adequately by any other grant mechanism available at NIH and are dedicated to areas of particular concern to NCI. The CEGP encourages innovative uses of the R25 grant to explore educational approaches that will help promote progress in preventing and curing cancer.

The CEGP grant applications can pursue a wide range of objectives from short courses, national forums, seminars, and/or hands-on workshops designed to educate scientists, health care professionals and the lay community; to the design, development and evaluation of new curricula of special significance to cancer in educational institutions; to structured short-term didactic and research experiences designed to motivate high school; college; and medical, dental and other health professional students to pursue careers in cancer research; to the development and evaluation of new educational methods and tools directed at different audiences with the intent of having an impact on reducing cancer incidence and mortality. The R25 can also be used to fund symposia and support rapidly evolving areas (e.g., courses in innovative screening).

Inquiries: Lisa Begg, Centers, Training and Resources Program, NCI, phone: 301 496-8580, e-mail: beggl@mail.nih.gov

PA-00-005: Midcareer Investigator Award in Patient-Oriented Research (K24)

Participating Institutes and Centers of NIH invite

applications for the Midcareer Investigator Award in Patient-Oriented Research (K24). The purpose of the award is to provide support for physicians to devote protected time to patient-oriented research and to act as mentors for beginning clinical investigators.

The award will enable candidates holding clinical doctoral degrees to undertake up to five years (a minimum of three are required) of patient-oriented research. Awards are renewable for one additional five-year period if the candidate still meets the stated requirements.

The overall goal of NIH is to support between 60 and 80 awards in fiscal year 1999 and in each succeeding year through fiscal year 2003. The actual number of awards to be made by each Institute or Center will vary yearly and will be dependent upon the number and quality of applications submitted and funds available.

The target candidates are outstanding clinical scientists who are actively engaged in patient-oriented research and are generally within 15 years of their specialty training. Candidates must be able to demonstrate the need for a period of intensive research focus as a means of enhancing their clinical research careers and must be committed to mentoring the next generation of patient-oriented researchers.

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. This area of research includes 1) mechanisms of human disease; 2) therapeutic interventions; 3) clinical trials, and; 4) the development of new technologies.

Inquiries: For NCI, Lester Gorelic or Andrew Vargosko, Office of the Deputy Director for Extramural Sciences, Office of Centers, Training and Resources, Executive Plaza North, Room 520, MSC 7390, Bethesda, MD 20892-7390, phone: 301 496-8580; fax: 301 402-4472; email: lg2h@nih.gov or av8b@nih.gov

PA-00-004: Mentored Patient-Oriented Research Career Development Award (K23)

The award is intended to support the career development of investigators who have made a commitment to focus their research endeavors on patient-oriented research. This mechanism provides support for three to five years of supervised study and research for clinically trained professionals who have the potential to develop into productive, clinical investigators focusing on patient-oriented research.

The project period may be for up to five years with a minimum of three years. Awards are not renewable. The overall goal of the NIH is to support approximately 80 competing awards in fiscal year 1999 and in each succeeding year through fiscal year 2003.

Inquiries: For NCI, Lester Gorelic or Andrew Vargosko, Office of the Deputy Director for Extramural Sciences, Office of Centers, Training and Resources, Executive Plaza North, Room 520, MSC 7390,Bethesda, MD 20892-7390,phone: 301 496-8580; fax: 301 402-4472; email: lg2h@nih.gov or av8b@nih.gov

PA-00-003: Mentored Clinical Scientist Development Award (K08)

The award is intended to support the development of outstanding clinician research scientists. This mechanism provides specialized study for individuals with a health professional doctoral degree committed to a career in laboratory or field-based research. Candidates must have the potential to develop into independent investigators. The K08 supports a three, four, or five year period of supervised research experience that may integrate didactic studies with laboratory or clinically-based research. The proposed research must have intrinsic research importance as well as serving as a suitable vehicle for learning the methodology, theories, and conceptualizations necessary for a well trained independent researcher.

Because of the focus on progression to independence, the prospective candidate should propose a period of study and development consistent with previous training and her/his career development needs. For example, a candidate with limited experience in a given field of research may find a phased developmental program lasting for five years which includes a designated period of didactic training and supervised research experience the most efficient means of attaining independence. A candidate with substantial previous research experience may require a shorter award period to facilitate the transition to independence.

The project period may be for three, four or five years and will depend upon the number of years of prior research experience, the need for additional experiences to achieve independence, and the policy of each particular institute or center. Awards are not renewable.

NCI uses this award mechanism exclusively for individuals with clinical doctoral degrees for career development in the basic sciences. Candidates do not need postgraduate clinical training and do not have to be board eligible to apply for this award.

Inquiries: For NCI, Lester Gorelic or Andrew Vargosko, Office of the Deputy Director for Extramural Sciences, Office of Centers, Training and Resources, Executive Plaza North, Room 520, MSC 7390, Bethesda, MD 20892-7390, phone: 301 496-8580; fax: 301 402-4472, email: lg2h@nih.gov or av8b@nih.gov

NCI Contract Award

Title: Radiation Dosimetry for Epidemiologic Studies.

Contractor: University of Texas/MD Anderson Cancer Center, $1,736,114.

In Brief:

Advice And Information Offered In Book For Cancer Survivors

(Continued from page 1)

NEW CANCER SURVIVORS, Living With Grace, Fighting With Spirit" is the title of a book by long-term cancer survivor, writer, and activist **Natalie Davis Spingarn**, published by Johns Hopkins University Press (http://www.press.jhu.edu or 800-537-5487). Spingarn, author of "Hanging In There," offers information and inspiration to survivors and medical professionals. . . . **PATIENT PROTECTION:** NCI said it has created a booklet and a web page designed to help researchers and the public understand how a Certificate of Confidentiality functions. First authorized by the Department of Health and Human Services in 1970 to protect participants in drug-abuse related studies, Certificates of Confidentiality empower principal investigators to refuse disclosure of sensitive research results about participants in research studies, even when responding to a court-ordered subpoena. These certificates now can protect not only individuals in drug studies, but also participants in behavioral and clinical research. NCI said it issues certificates sparingly for single, well-defined projects and for cooperative multi-site studies. Copies of "Certificates of Confidentiality: Background Information and Application Procedures" are available by calling 1-800-4-CANCER; or online at http://cancertrials.nci.nih.gov (click on "Resources"). . . **JOHN MENDELSOHN**, president of M.D. Anderson Cancer Center, received the Jill Rose award from the Breast Cancer Research Foundation Oct. 21. The award is given for research leading to improved therapies for breast cancer. . . **YALE CANCER CENTER** received a second pledge of $500,000 to support lymphoma research from the Ted Mann Foundation of Los Angeles. . . **KATHRYN CONRAD**, program leader for Cancer Education and Standards Integration for the University of Pittsburgh Cancer Institute, received the 1999 Distinguished Service Award from the NCI Cancer Patient Education Network. The award is presented for outstanding contributions to the practice and profession of cancer patient education. . . . **REPS. MATT SALMON** (R-AZ) and **JOHN SHADEGG** (R-AZ) received the first Medal of Honor from US Oncology, a physician practice management company based in Houston, TX. The award is presented to members of Congress in recognition of their work for a stronger cancer care delivery system. . . **VINCENT DEVITA** has received the 1999 Mary Waterman Award from the Breast Cancer Alliance of Greenwich. DeVita, former NCI director (1980-88), is director of the Yale Cancer Center. . . **DORIS DUKE CHARITABLE FOUNDATION** awarded $6 million to two cancer researchers for Bench to Bedside Research. Each will receive $3 million over a five-year period to provide a stable source of funding for their clinical research. The awardees are **Kenneth Anderson**, Dana-Farber Cancer Institute, for development of novel treatment approaches for multiple myeloma; and **David Scheinberg,** Sloan-Kettering Cancer Center, for cancer immunotherapies which selectively target neoplastic cells while sparing normal cells and tissues. . . . **NCI AWARDED** more than $1 million to a new partnership between Meharry Medical College and Vanderbilt-Ingram Cancer Center for research and patient care initiatives to help close the gap between blacks and whites in cancer incidence and deaths. The award is a supplement to the Vanderbilt-Ingram Cancer Center Support Grant. . . . **CANCER MARCH IN JORDAN:** More than 50,000 Jordanians marched in Amman, Jordan, on Oct. 22, to raise funds for cancer treatment as a tribute to the late **King Hussein**, the Associated Press reported. **Queen Noor**, Hussein's American-born widow, led the seven-mile march across the Jordanian capital, accompanied by members of the ruling Hashemite dynasty and entertainers from Egypt, Syria, Kuwait, and Jordan. "Hussein's First March of Hope" was named for the late monarch, who died of cancer last February at age 63. Participants wore t-shirts which sold for one Jordanian dinar ($1.40) and featured a portrait of Hussein. The funds raised from the t-shirt sales will go to Al-Amal Hospital.

Letter to the Editor:

"Wonderful" Humor On Bands

It's hard to get humor into a publication such as **The Cancer Letter**, but your piece in the Oct. 15 issue under the new category of NIH Entertainment Report ("Hopkins Band Wins First Place On The Directors' Home Turf") was wonderful. Congratulations! Keep up the good work that yields such a readable and helpful publication.

Moody Wharam Jr.

Professor of Oncology, Radiological Sciences, Neurosurgery and Pediatrics, and Director, Division of Radiation Oncology, Johns Hopkins Oncology Center

THE CANCER LETTER

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Business & Regulatory Report

Formerly "Cancer Economics"

Oncology Management:

Medtronic To Support NCCN Development Of Oncology Outcomes Database In Pain

Medtronic Inc. (NYSE: MDT) of Minneapolis said it will give **National Comprehensive Cancer Network** up to $525,000 over three-years to support the development and expansion of the Oncology Outcomes Database to measure adherence to the network's pain control guidelines.

The NCCN database will provide information about pain therapies administered under the network's cancer pain treatment guidelines for comparisons of techniques and outcomes. Initial data from this first-of-its-kind national database are expected in about 18 months.

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Clinical Trials:

Enrollment Completed In Phase III Trial Of Therapeutic Melanoma Vaccine GMK

Progenics Pharmaceuticals Inc. (Nasdaq: PGNX) of Tarrytown, NY, and **Bristol-Myers Squibb Co.** have reached full enrollment in the phase III clinical trial of GMK, a therapeutic cancer vaccine for the treatment of malignant melanoma.

Eastern Cooperative Oncology Group is conducting the trial with participation by the Southwest Oncology Group, the Cancer and Leukemia Group B, the North Central Cancer Treatment Group and the M.D. Anderson Cancer Center. The trial compares GMK vaccine to high-dose alpha interferon, the companies said. The study, the largest ever performed in melanoma, has enrolled over 850 patients at approximately 300 medical centers in the US, the companies said.

Progenics and BMS said they are collaborating on the development of GMK vaccine under an agreement initiated in 1997, in which BMS was granted an exclusive worldwide license to the product. A second cancer vaccine, MGV, is also being developed as part of the collaboration. MGV is entering phase II clinical trials and is being developed for application in a variety of cancers.

"This clinical trial with GMK is significant not only because of its size but more importantly because this is the first vaccine using a well-defined melanoma antigen capable of producing a specific immune response," said John Kirkwood, principal investigator of the study, chairman of the Melanoma Committee of ECOG, and professor in the division of medical oncology at the University of Pittsburgh. "If the outcome of this clinical trial is positive, the GMK vaccine may represent the first

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

NCCN To Compile Information On Pain And Quality Of Life

(Continued from page 1)

The NCCN database will compile information on pain and quality of life before, during and after cancer therapy. The database also will collect and analyze data on how physicians adhere to the updated version of NCCN guidelines for the management of cancer pain and how patients benefit from the provision of a range of pain therapies.

"This agreement with Medtronic affirms the critical importance of the NCCN's Oncology Outcomes Database," said William McGiveny, CEO of NCCN. "It also reflects our shared commitment to the highest quality of cancer care through excellence in research and the collection and analysis of outcomes data."

Studies have targeted undertreatment of pain as a significant problem in cancer care. When measured against standards set forth by the federal Agency for Health Care Policy and the World Health Organization, one study found that nearly half (46 percent) of cancer patients were undertreated with respect to use of analgesics. Another study suggested that the problem is worse in minority cancer patients, with 60 percent of African-Americans and Hispanics undertreated for pain.

A recent survey by the American Society of Clinical Oncology found that there are still critical gaps in the treatment of cancer patients at the end of life. The survey of 3,300 oncologists found that physicians are eager for increased professional education and access to palliative care services.

The NCCN, established in 1995, is a coalition of 17 leading U.S. cancer treatment centers. Its Oncology Practice Guidelines offer clinical policy for the care of more than 90 percent of all cancers. The database now includes information about more than 2,000 cancer patients.

"The effective treatment of cancer must be the highest priority, but we are pleased that the NCCN shares our interest in also focusing on pain management and the improvement of patients' quality of life during the treatment process," said Scott Ward, vice president and general manager of Drug Delivery in Medtronic Neurological and Spinal.

Medtronic SynchroMed, an implantable drug infusion system introduces in 1991, delivers controlled doses of pain medication.

* * *

Fox Chase Cancer Center said it has formed a partnership with Hospital do Cancer/Fundacao Antonio Prudente, of Sao Paolo, Brazil, to identify opportunities for cooperation.

Fox Chase said the goals of the partnership include: developing oncology specific clinical and research education training; implementing advanced systems for clinical trial management that enhance reporting, bio-statistics and development of study designs; collaborating on research projects in basic and population science; and seeking business ventures.

The memorandum of understanding, signed by both parties, serves as a beginning in their agreement to exchange expertise, the company said.

Philadelphia International Medicine will facilitate strategic implementations with full recognition by Hospital do Cancer that PIM is Fox Chase's international business development partner. PIM links greater Philadelphia's hospitals with physicians and medical technology to made comprehensive, quality healthcare available to patients in the international community.

In another development, Conemaugh Health System of Johnstown, PA, has joined the Fox Chase Network, a group of 21 community hospitals in Pennsylvania and New Jersey working cooperatively with Fox Chase Cancer Center. The affiliation creates the Conemaugh Center for Cancer Care, a joint program of Conemaugh and Fox Chase.

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The network, which was formed 13 years ago, has put more than 2,500 patients on clinical trials throughout Pennsylvania and New Jersey, Fox Chase officials said.

* * *

SuperGen Inc. (Nasdaq: SUPG & SUPGW) of San Ramon, CA, said it has formed a clinical and business relationship with **US Oncology** to carry out clinical programs using the company's rubitecan and Nipent anticancer compounds.

Rubitecan is in phase III studies in the US and Europe for the treatment of pancreatic cancer. Data from a phase II study of rubitecan conducted by SuperGen's licensor, the Stehlin Foundation for Cancer Research in Houston, was published in the May issue of the International Journal of Oncology. Another trial of rubitecan, for myelodysplastic syndrome/chronic myelomonocytic leukemia, is underway at M.D. Anderson Cancer Center.

Nipent, currently approved and marketed by SuperGen for the treatment of hairy cell leukemia, is also in late-stage clinical testing for the treatment of a variety of lymphomas, acute leukemias and hematological malignancies. Opinion leaders from all over the world, meeting at the recent Pan-Pacific Lymphoma Conference, urged that clinical studies of combination treatment with Nipent for use in earlier stages of low-grade lymphoma begin immediately.

* * *

WakeMed of Raleigh, NC, a healthcare system, said it has entered into a collaborative agreement with **nTouch Research Corp**., a clinical trials services provider.

nTouch will assume all ongoing clinical studies conducted by the WakeMed Clinical Research Institute and will manage other clinical research activities for WakeMed. The relationship is expected to expand the research role of WakeMed and increase the value of clinical research to its physicians and patients, the company said.

Clinical Trials:

Companies Plan To Accelerate Trials Of Melanoma Vaccine

(Continued from page 1)

vaccine approved for any form of cancer," he said.

The companies said they plan to accelerate clinical development of GMK vaccine outside of the U.S. by integrating a second ongoing phase III study in high-risk melanoma with a scheduled third phase III trial in patients with intermediate-risk disease. This trial will be sponsored by BMS and will include investigators from the European Organization for the Research and Treatment of Cancer, Australia, South America, and South Africa.

The GMK vaccine is designed to stimulate a patient's immune system to control or eradicate residual cancer cells after the tumor has been resected. GMK incorporates the Gm2 ganglioside, a cancer antigen present in approximately 95 percent of melanoma cells. Phase I/II studies showed that vaccination of melanoma patients with GMK resulted in the formation of antibodies against Gm2 capable of killing melanoma cells. Patients with high-risk melanoma who have antibodies against Gm2 remain disease free for significantly longer periods and have longer overall survival, the company said.

* * *

AEterna Laboratories (ME, TSE: AEL) of Quebec, said it will accelerate the clinical development of its antiangiogenic drug AE-941/ Neovastat. Aeterna will initiate more oncology trials, in addition to the phase III trial in non-small-cell lung cancer sponsored by NCI, the company said.

"By targeting cancers for which there is currently very limited therapies available, we will be able to seek an earlier approval with the regulatory agencies after a successful trial. The first trial will be initiated in renal cell carcinoma patients,'' said Yves Rosconi, senior vice president and CEO of AEterna. "From our phase I/II trials, we have observed encouraging results especially in some RCC patients and feel optimistic about the outcome of this new trial.''

* * *

Celsion Corp. (OTC BB:CELN), of Columbia, MD, and **Columbia/HCA Healthcare Corp**., said its breast cancer treatment system has been installed at a Columbia/HCA member hospital in West Palm Beach, Florida, which is now recruiting patients for phase I clinical studies of Celsion's system.

To expedite patient accrual and accelerate the trials, phase I clinical studies of its breast cancer treatment will begin at Harbor UCLA Medical Center in California, the company said.

The phase I trials will evaluate the safety of Celsion's focused heat treatment system, designed to destroy cancerous tumors and viable cancer cells using heat alone. The device is a thermotherapy delivery system that will offer a non-surgical, minimally invasive, non-toxic and side effect free

treatment, the company said.

Celsion said its treatment system incorporates the Adaptive Phased Array focusing technology that was developed by MIT and is exclusively licensed worldwide to Celsion.

* * *

ImClone Systems Inc. (Nasdaq: IMCL) of NY, said it has initiated patient treatment in a multi-center phase II clinical trial evaluating C225, a cancer therapeutic, in combination with CPT-11 in 98 patients with refractory colorectal carcinoma.

C225 is a monoclonal antibody that is an antagonist to the epidermal growth factor receptor, which is associated with the growth and survival of cancer cells in a variety of solid tumors, including colorectal, pancreatic and squamous cell head and neck carcinomas, the company said.

ImClone said it has initiated two phase III trials evaluating C225 in combination with chemotherapy or with radiotherapy for advanced squamous cell head and neck carcinoma. The company said it has also initiated a phase II trial evaluating C225 in combination with chemotherapy for refractory advanced squamous cell head and neck carcinoma.

* * *

Lifeline BioTechnologies Inc. (OTC BB: LBTI) of Reno, NV, will begin phase III clinical studies of its First Warning Breast Cancer Detection System. First Warning is exactly what the name implies, the warning of a potential problem.

Pilot studies indicate that Lifeline has discovered an inexpensive, non-invasive method for detecting angiogenic activity related to breast cancer growth, the company said. The marker will identify women who are in need of further diagnostic testing, the company said.

Lifeline said it plans to initiate phase III clinical studies in January.

* * *

Matrix Pharmaceutical Inc. (Nasdaq: MATX) of Fremont, CA, said it has closed enrollment in the phase II clinical trial of FMdC in non-small cell lung cancer because of the application of a predetermined stopping rule.

Preliminary analysis does not show meaningful clinical activity with FMdC as a stand-alone therapy in this indication at the dose and regimen tested. The phase II clinical trial of FMdC in colorectal cancer is continuing to accrue patients, the company said.

FMdC is a systemically administered chemical entity and is a member of a class of chemotherapeutics called nucleoside analogues that have shown efficacy in treating various types of cancers. Nucleoside analogues have been used both as stand-alone therapies and in combination with other anticancer drugs, the company said.

In addition to FMdC, Matrix is developing IntraDose (cisplatin/epinephrine) Injectable Gel.

IntraDose, the company's lead product candidate, is completing phase III studies for the treatment of head and neck cancer and phase II studies in primary and metastatic liver cancer. IntraDose is injected directly into tumors.

Matrix Pharmaceutical said it is developing MPI 5020, a locally injected gel containing the anticancer agent fluorouracil, which is in a phase I/II trial in recurrent and metastatic breast cancer.

* * *

York Medical Inc. of Mississauga, ON, said it has received approval from the Health Protection Branch of Canada to begin a phase I/II clinical trial for TheraCIM-h-r3, its immunotherapeutic anti-tumor agent. TheraCIM-h-r3 is a humanized monoclonal antibody directed against the epidermal growth factor receptor.

York Medical said the study is designed to demonstrate preliminary efficacy and safety of TheraCIM-h-r3 in conjunction with radiotherapy in patients with locally recurrent or metastatic squamous cell carcinoma of the head and neck. There are 16 patients in the study that will be conducted at the London Regional Cancer Centre London.

Together with its joint venture partner, the Centre of Molecular Immunology in Havana, York Medical said it is developing a family of oncology products based on this monoclonal antibody targeting solid tumours including head, neck, breast and lung.

TheraCIM is the third product from this family to enter clinical trials in Canada. An anti-cancer vaccine utilizing recombinant human EGF is in a pivotal trial in patients with non-small cell lung cancer at the London center.

A study with DiaCIM, designed to identify tumors over-expressing EGF-r, is being conducted at The Princess Margaret/Toronto Hospitals in Toronto, the company said.

The company will begin another application for a clinical trial for its targeted radiotherapeutic using the same monoclonal antibody. All of the humanized monoclonal antibody products were originally developed by CIM and are in various stages of clinical evaluation in Cuba.

Product Approval & Applications:

FDA Grants Fast Track Status To Neurocrine's IL-4 Compound

Neurocrine Biosciences Inc. (Nasdaq: NBIX) of San Diego, said FDA has granted Fast Track designation to the IL-4 Fusion Toxin compound (NBI-3001). Neurocrine Biosciences is conducting a phase II trial to assess safety and determine the maximum tolerated dose.

Twenty-two patients have been treated, the product appears to be well tolerated and the mtd has been determined. The ongoing phase II clinical trial will bridge into the phase III pivotal trial in the first half of next year, the company said.

Friedrich Weber, principal investigator for the European phase II clinical program for NBI-3001, said patient MRI scans displayed dramatic changes suggestive of tumor necrosis, indicating NBI 3001 has a robust anti-tumor effect. He presented these preliminary results at the13th International Conference on Brain Tumor Research and Therapy.

FDA guidelines include a six-month goal for the review of new product applications identified as Fast Track. The Fast Track review process was authorized by the FDA Modernization Act of 1997 to expedite the review of treatments that have the potential to address unmet medical needs for serious life-threatening disease.

Preclinical data suggest that when infused directly into the glioblastoma, IL-4 Fusion Toxin kills the tumor cell but not the healthy brain cells, the company said.

IL-4 Fusion Toxin is a protein in which a blood cell derived growth factor (IL-4) has been joined with a Pseudomonas exotoxin, a potent toxin that can destroy cancer cells. IL-4 has very high affinity for-IL-4 receptors, which are highly localized on malignant brain tumors, but do not exist, on normal brain cells.

IL-4 binds tightly to the IL-4 receptors on the surface of the glioblastoma cells and delivers the exotoxin directly into the cell, resulting in cell death, the company said. IL-4 Fusion Toxin is administered via catheter that permits delivery directly into the brain tumor, the company said.

* * *

TriPath Imaging Inc. (Nasdaq: TPTH), of Burlington, NC, formerly NeoPath and AutoCyte, said it has submitted to FDA a supplement to the existing PMA for the AutoPap Primary Screening System to remove the current labeling limitation for processing thin-layer specimens on the AutoPap System.

TriPath's PMA supplement provides clinical data intended to demonstrate the performance of the AutoPap System as a primary screener for AutoCyte Prep System thin-layer preparations, the company said.

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Vion Pharmaceuticals Inc. (Nasdaq: VION) of New Haven, CT, said it has received investigational review board approval to begin a phase I safety trial of VNP20009, the first generation of TAPET (tumor amplified protein expression therapy) in cancer patients with stage IV melanoma or metastatic breast cancer patients with cutaneous metastases.

Vion Pharmaceuticals said the trial will be conducted at the Cleveland Clinic, and led by Ronald Bukowski.

Emerging Technologies:

Nexell Develops System For Dendritic Cell Processing

Nexell Therapeutics Inc. (Nasdaq: NEXL) of Irvine, CA, said it has developed clinical scale, closed system processes using the Isolex 300i Stem Cell Selection System and SteriCell culturing bags to generate dendritic cells from either monocytes or CD34+ cells.

Results from two separate laboratory studies were presented at the 6th International Workshop on Langerhans Cells in New York earlier this month.

"There is a great deal of excitement about the potential for using dendritic cells to focus patients' immune systems on attacking tumor cells," said Michael Lotze, codirector of biologic therapeutics at the University of Pittsburgh Cancer Institute and a plenary speaker at the workshop. "We are in the process of evaluating these cells in early phase clinical trials designed to study the benefits of dendritic cell therapy."

Dendritic cells pick up foreign antigens and presenting them in the appropriate way to T-cells, thereby triggering an immune response. Because they play this central role in controlling immunity, dendritic cells have become the main focus of many experimental approaches to the treatment of cancer and infectious disease. To stimulate the immune system to attack cancer cells, several investigators are generating dendritic cells outside the body and

then loading them with tumor antigen, DNA for tumor antigen or enhancers of the immune system so the cells are able to present the tumor antigen efficiently to immune system T-cells.

If the therapeutic approach works, patients could be vaccinated against their own cancer by chronic stimulation of their immune response to the tumor through periodic infusion of dendritic cells. The dendric cells would be selectively and specifically primed with tumor antigen, the company said.

Although there are several pathways for generating dendritic cells, those derived from CD34+ cells are more effective in presenting antigen. In one of the Nexell studies, mobilized apheresis products were enriched for CD34+ cells using the Isolex 300i Cell Selection System. The cells were then successfully cultured in SteriCell closed system gas permeable containers to generate dendritic cells. The study defines an efficient closed system process for generating dendritic cells from CD34+ cells, the company said.

In the second study, non-mobilized apheresis product was depleted of CD2+ and CD19+ cells with the Isolex 300i to produce an enriched population of CD14+ monocytes, the more common source for cultured dendritic cells. This process was completed in 2.5 hours as compared to 8 to 10 using current methods of cell adherence at this scale. Dendritic cells were then successfully cultured in closed SteriCell containers. This second method also resulted in a dendritic cell preparation with fewer contaminating T-cells and a greater ability to stimulate an in vitro immune response, the company said.

"We have been able to show that by culturing Isolex enriched cells in SteriCell containers we can efficiently generate high quality dendritic cells in large quantities," said Dennis Van Epps, vice president of research at Nexell Therapeutics. "By using these closed, gas permeable containers, we have also minimized contamination risks associated with open culture systems," he said.

The Isolex 300i Cell Selection System is marketed in the U.S. for the selection of hematopoietic stem cells and the removal of tumor cells from autologous peripheral blood as a component of aggressive cancer therapy, the company said.

Isolex cell selection systems are also marketed in the European Union and Canada and are available for use in Hungary, Israel, New Zealand, Poland, and Slovenia. Nexell said it is seeking clearance to market the Isolex systems in Australia, Japan and various countries in Eastern Europe and the Mediterranean region.

* * *

ChromaVision Medical Systems Inc. (Nasdaq: CVSN), San Juan Capistrano, CA, said the NCI Division of Basic Sciences will purchase the company's ACIS imaging system.

The company said the system would be used in an NCI study of the possible link between a carcinogenic chemical and human esophageal cancer risk in a region of China where the mortality from esophageal cancer is exceptionally high.

"ACIS allows us to quantify changes in the cell that may uncover the causes of certain cancers," said Miriam Poirier, head of the Carcinogen-DNA Interactions Section of NCI. "We will be using the ACIS to detect cellular changes that could lead to early detection of esophageal cancer." Poirier said ACIS could be used for quantification of any signal within cells of interest and would be useful for many applications in the laboratory.

ChromaVision said NCI is conducting a study to determine the possible association of exposure to polycyclic aromatic hydrocarbons and esophageal cancer. To analyze a large bank of samples, NCI needed to select an instrument with high accuracy and throughput.

Deals & Collaborations:

Cytogen To License RCAT From Molecular Staging Inc.

Cytogen Corp. (Nasdaq: CYTO) of Princeton, NJ, said it has signed a letter of intent to obtain an exclusive, worldwide license from **Molecular Staging Inc.** of Guilford, CT, for the Rolling Circle Amplification Technology.

The technology will be used to develop in vitro diagnostic tests for Prostate Specific Membrane Antigen and Prostate Specific Antigen, Cytogen said.

Like PSA, PSMA is increased in prostate cancer. However, unlike PSA, PSMA does not appear to be affected by other events, the company said.

Cytogen said it plans to use RCAT to develop a PSMA and PSA test for prostate cancer. An assay for clinical study should be available next year, the company said. The company plans to evaluate assays to diagnose other tumors where PSMA is found in the associated neovasculature. For concept testing and clinical evaluation of these various assays, Cytogen will draw on its collaboration with Bostwick

Laboratories of Richmond, VA.

RCAT, a process discovered at Yale University School of Medicine, is based on a method of highly efficient amplification that enables the detection of target molecules in a wide array of testing formats. Cytogen said it considered several technologies for use in this project, and selected RCAT over other alternatives, including RT-PCR technology, because of RCAT's advantages in solid phase recognition, amplification and detection of target molecules either directly on a cell or biochip, the company said.

According to industry estimates, over $400 million is now spent on PSA testing in the US. In two-thirds of men with an elevated PSA the cause is something other than cancer.

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Draxis Health Inc. (TSE: DAX; Nasdaq: DRAX) of Mississauga, Ontario, said its radiopharmaceutical subsidiary, Draximage Inc., signed an agreement with **Isogenic Science Ltd.** for the exclusive rights to brachytherapy seeds technology.

Draxis Health said the license entitles Draximage to manufacture and market Iodine-125 brachytherapy seeds in North America. Draximage will make an upfront payment to Isogen and pay a royalty based on sales. Draximage has been given the option to license the I-125 seeds for other territories; it has also been given rights to additional products developed by Isogen.

Draximage said it would manufacture the I-125 seeds within its radiopharmaceutical lab in Kirkland, Quebec.

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Genentech Inc. (NYSE:DNA) of South San Francisco, said **Roche Holdings Inc.** intends to sell in an underwritten public offering 20 million shares of Genentech common stock

The shares represent 15.6 percent of the outstanding common stock of Genentech. Roche will grant the underwriters an option to purchase an additional two million shares to cover over-allotments. Roche's economic and voting ownership of Genentech will be reduced to approximately 65 percent, the company said.

Genentech said proceeds from the proposed offering will be for the sole benefit of Roche, with Genentech receiving no proceeds from this transaction. Concurrently, Roche intends to issue U.S. dollar denominated bonds exchangeable with Roche for up to approximately 5.5 million shares of Genentech common stock owned by Roche.

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Isis Pharmaceuticals (Nasdaq: ISIP) of Carlsbad, CA and Collegeville, PA, and **Rhone-Poulenc Rorer** (NYSE: RP) said they signed a three-year collaboration to assess genes identified within RPR's genomics programs using Isis' Antisense Target Validation technology.

Isis and RPR said the collaboration will enable RPR to determine the function and therapeutic value of numerous novel gene targets and to use the information about gene function to develop pharmaceutical products. It also provides Isis with valuable information on targets to assist in the development of novel antisense drugs.

RPR will provide Isis with sequence information on novel gene targets. RPR has an option to expand the number of gene targets. Using its proprietary Rapid Throughput Screening technology, Isis will design optimized antisense inhibitors for these targets, the companies said.

RPR will use these antisense inhibitors to identify the function of the gene, its role in molecular pathways associated with the disease, and prioritize the gene targets for development. Isis will develop antisense inhibitors for the targets provided by RPR. RPR will pay Isis research fees and milestone payments based on the success of the program.

The companies said the agreement allows Isis access to numerous novel genes identified within the RPR portfolio for use in developing antisense products. RPR said it will utilize Isis technology to elaborate on the function of these genes.

* * *

Millennium Pharmaceuticals Inc. (Nasdaq: MLNM) of Cambridge, MA, and **Bayer AG**, of Leverkusen, Germany, said they have identified 18 novel drug targets and moved four of them into high throughput screening in less than eight months.

The alliance has achieved its efforts to industrialize the drug discovery process by employing a new model to rapidly identify, validate and screen "drug targets," the companies said. The targets were identified and validated by Millennium and are being screened by Bayer.

The alliance is pursuing a novel production-oriented approach, based on genomics research, to rapidly move compounds toward clinical trials. Millennium integrates large-scale genetics, genomics, automation, informatics, and drug discovery technologies which enables it to simultaneously

identify thousands of new genes, investigate their application in drug discovery and perform focused searches for disease-relevant targets and leads for drug development, the companies said.

The drug targets identified are then incorporated directly into test systems and used in the search for lead compounds with the aid of Bayer's high-throughput robot screening technology. This screening process is capable of testing more than 100,000 substances each day, the companies said.

The companies said the alliance, which began in September 1998, is believed to be the largest to date in the field of pharmaceutical drug discovery. In return for a total investment of up to $465 million, including approximately 14% equity investment in Millennium, over a five-year period Bayer receives access to key technologies in modern genome research and a flow of new genomics-based targets for drug development.

The goal of the five-year alliance is for Millennium to supply 225 "drug targets" identified as relevant for cardiovascular disease, cancer, osteoporosis, pain, liver fibrosis, hematology and viral infections.

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Myriad Genetics Inc. (Nasdaq: MYGN) of Salt Lake City said it has identified six targets for drug discovery and has designed assays to detect small molecule drugs modifying these targets. High-throughput drug screens have begun against the first three of these targets using a diverse library of low molecular weight chemical compounds to isolate lead compounds for further drug development.

The initial targets were identified using the company's ProNet technology, which discovers drug targets by mapping protein interactions and identifying the members of disease pathways. The drug targets in high-throughput screening are all key regulators of important disease pathways. Myriad Pharmaceuticals is screening for compounds to treat cancer and rheumatoid arthritis. The company said it would screen for compounds to treat atherosclerosis, chronic pain and certain central nervous system diseases.

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Novavax Inc. (Amex: NOX) of Columbia, MD, said NCI has awarded a contract to its Biomedical Services Division in Rockville, MD, to manufacture recombinant chimeric virus-like particle vaccines against human papilloma virus. The vaccine candidates would be designed to prevent or treat HPV infections that cause cervical cancer.

Novavax said the HPV vaccines were developed by research and development teams lead by Robin Robinson, associate director of NBSD and Douglas Lowy, Laboratory of Cellular Oncology at the NCI. Robinson will serve as principal investigator on the new HPV vaccine project for Novavax.

* * *

Select Therapeutics Inc. (OTC BB: SLPU) of Cambridge, MA, said a toxin produced by E. coli bacteria has been used to rid bone marrow of cancer cells for the first time. The finding came from research teams at Princess Margaret Hospital's Ontario Cancer Institute, the Cross Cancer Institute and the University of Alberta.

The toxin could be effective in completely purging all traces of cancer in a patient's stem cell graft, greatly improving the success of autologous stem cell transplants in patients with some cancers, the company said.

Jean Gariepy, of Princess Margaret Hospital, pioneered the technique aimed to reduce the likelihood of re-infusing diseased cells back into patients suffering from breast cancer, lymphoma and multiple myeloma, the company said.

Select Therapeutics said the researchers are using a toxin called SLT-1 to clean blood cells of cancer cells by using a receptor on the surface of the cancer cells recognized by the toxin. The toxin is removed from blood cells prior to re-infusing the stem cells back into cancer patients. The researchers found that while the toxin kills a broad range of cancer cells, particularly breast, lymphoma and multiple myeloma cells, it does not kill healthy blood stem cells.

Select Therapeutics said it entered into a license and research agreement with the Ontario Cancer Institute and the University of Toronto Innovation Foundation last year to develop improved autologous stem cell transplantation therapies. The license grants Select exclusive worldwide rights to use the invention, and manufacture products based on the invention, in return for royalties and research support to the Ontario Cancer Institute, the company said.

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TriPath Imaging Inc. (Nasdaq: TPTH) of Burlington, NC, said it has entered into a business alliance with **Pathology Service Associates Inc.** to offer the AutoCyte PREP System to PSA's affiliated pathology practices for routine use in cervical cancer screening.

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