THE CANCER LETTER INTERACTIVE

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

Vol. 25 No. 46
Dec. 3, 1999

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Price $275 Per Year

# Review Group Urges Increased Funding For NCI AIDS Drug Discovery Program

NCI's AIDS drug discovery and development program is under "severe financial restraint" and faces "organizational challenges" that include a lack of coordination of basic and clinical research, according to a new report to the Institute.

Based on a previous report on NIH AIDS programs convened by the Office of AIDS Research Advisory Council in 1995, NCI began a rapid down-scaling of its in vitro cell-based screen of natural products and synthetic compounds.

Although instrumental early in the AIDS epidemic, primary HIV

(Continued to page 2)

*In Brief:*

## Washington University, Barnes-Jewish To Combine Cancer Programs In New Center

**WASHINGTON UNIVERSITY** School of Medicine and Barnes-Jewish Hospital in St. Louis received a $35 million endowment for cancer research, patient care and services, and education and community outreach from Alvin and Ruth Siteman. The endowment includes the $10 million cancer-related gift given to Barnes-Jewish in 1997. Washington University and Barnes-Jewish will name their combined cancer programs the Alvin J. Siteman Cancer Center. . . . **V. CRAIG JORDAN** was named the Diana, Princess of Wales, Professor of Cancer Research at Northwestern University. Jordan is professor of cancer pharmacology at Northwestern University Medical School and director of the Lynn Sage Breast Cancer Research Program affiliated with the Robert H. Lurie Comprehensive Cancer Center at Northwestern. Chicago philanthropist Ann Lurie funded the endowed chair in memory of Princess Diana, who visited Northwestern in 1996 as the keynote speaker in a symposium on breast cancer. Lurie is a member of the university board of trustees. . . . **WILLIAM DALTON** was appointed deputy director of H. Lee Moffitt Cancer Center and Research Institute at the University of South Florida. Dalton is associate center director for clinical investigations and chairman of the Interdisciplinary Oncology Program. **W. MICHAEL ALBERTS,** leader of the Thoracic Oncology Program at Moffitt, was appointed chief medical director/associate center director for clinical affairs. **KAREN FIELDS** was named medical director of affiliation and referring physician relations at Moffitt. Fields is leader of the Moffitt Blood and Transplant Program.

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# NCI, NIAID, OAR Form Group To Coordinate AIDS Research

(Continued from page 1)

drug cell-based screening was no longer contributing to the more recent development of antiviral agents, according to the final draft report of the Developmental Therapeutics Program AIDS Review Group.

As a result, AIDS-related expenditures in the NCI Developmental Therapeutics Program fell from $20 million in fiscal year 1996, or 49 percent of the program's total budget, to $2 million in FY1999, or 6 percent of the program's budget, the latest report said. The proportion of AIDS funding is expected to fall to 4 percent of the DTP budget this fiscal year, the report said.

"With a budget of only $2 million, however, it becomes difficult to comprehend how DTP can be expected to accomplish any drug discovery mission within the field of HIV/AIDS therapeutics," the report said.

The report, presented last month to the NCI Board of Scientific Advisors, encourages the Institute to continue to fund an AIDS drug development program, emphasizing the new high-throughput molecular target-based assays.

"In many ways, AIDS research programs are anomalous within NCI; they exist because of historical events and funding patterns," the report said.

THE CANCER LETTER

Member, Newsletter Publishers Association

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**
**PO Box 40724, Nashville TN 37204-0724**

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**Founded Dec. 21, 1973, by Jerry D. Boyd**

"The Review Group carefully considered whether it continues to make sense to maintain the programs as they currently exist. The Review Group concluded that because the infrastructure for cancer drug discovery and development exists currently within the NCI DTP, and because of the critical importance of such a presence within NIH, it makes sense to maintain an AIDS program within NCI. However, its continued operation requires some reorganization, less insularity, and a better system of external review and oversight."

NCI also should conduct research in the development of drugs for AIDS-related cancers, the report said. "NCI currently is not involved in the discovery and development of new agents in AIDS malignancies and the involvement of industry appears to be limited," the report said.

The report called the administrative organization of DTP "problematic."

Intramural and extramural HIV/AIDS activities "appear fragmented," the report said. "In addition, there appears to be a lack of interactive collaborations, which seem to exist organizationally within NCI. Programs involving clinical sciences, HIV drug discovery, and basic science do not appear to be complementary. Thus, in addition to severe financial restraints on the relevant DTP research budget, there are organizational challenges to be addressed."

**Attempt To Integrate NIH Programs**

NCI officials said that based on the report's recommendations, they have formed a working group involving the National Institute of Allergy and Infectious Diseases and the NIH Office of AIDS Research to better coordinate and fund research, and divvy up responsibilities based on the strengths of each entity. NCI's strengths include repositories, informatics, toxicology, pharmacology, and screening, said Ellen Feigal, deputy director of the NCI Division of Cancer Treatment and Diagnosis.

Rather than viewing AIDS drug discovery and development as an insular unit within DTP, the new effort should be seen as an NIH integrated program, Feigal said to the BSA. NCI and NIAID have a long history of informal interactions and joint collaborations in this area, and this new report catalyzes the efforts to become more formally coordinated, she said.

The OAR advisory group will likely serve as the outside expert group overseeing the work of the NIH integrated AIDS drug discovery and



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development program, Feigal said.

Once the scientific merit of an application seeking support for the development of a new agent has been established, an internal working group would then decide which Institute would provide the funding or resources, Feigal said. Initially, NCI funding for DTP will remain at the current level until the Institute gets a better idea of the demand, she said.

Carl Dieffenbach, NIAID scientific director, said that the Institutes originally divided responsibilities for HIV/AIDS therapeutics in 1984 and 1985. "We always felt our best effort was in developing new concepts for therapeutics, and in phase III clinical trials," he said to the BSA.

"Over time, the Cancer Institute built up a large portfolio in drugs, medicinal chemistry and synthesis, and in pharmacology/toxicology. From the NIAID perspective, we focused on target identification and limited support for preclinical development through contract mechanisms."

**Report Recommendations**

NCI has not yet published the report of the Developmental Therapeutics Program AIDS Review Group or posted the text online. Following are the report's major recommendations:

1. NCI should establish a single Scientific Advisory Board consisting of both extramural scientists from academia and industry and leaders in the intramural program to review and provide oversight of DTP activities on a quarterly basis.

2. The focus of AIDS drug discovery within the DTP should be in the development of non-cell-based, high-throughput, new target-based assays, grounded in research performed within NCI and in collaboration with academia with emphasis on targets that are not being actively pursued by industry.

3. Cell-based assays should be used primarily as secondary assays to confirm hits or leads from molecular and biochemical assays.

4. Use of synthetic compound libraries and purified discrete natural product libraries for primary screening in cell-based assays should be continued on a limited basis.

5. NCI should continue to maintain, replenish, and expand its existing repository of natural product extracts for drug discovery.

6. NCI should acquire and build combinatorial small molecule chemical libraries for intramural and extramural use in mechanism- and cell-based screening for AIDS therapeutics.

7. NCI should seek advice in the form of an external advisory group of experts to address issues of chemical diversity, new target-based assays, development of methods for the selection and prioritization of compounds for screening, and supervision of the natural products library and libraries constructed using combinatorial chemistry approaches.

8. NCI should implement state-of-the-art methods for data management of its libraries and compounds and of results derived from use of these libraries in various screens. Methods to improve access by the extramural community to DTP resources should be implemented.

9. DTP should have the medicinal chemistry capability required to optimize leads generated by screening or structure-based design strategies against novel HIV or opportunistic infections targets.

10. DTP should play a transitional role in identifying industrial partners to optimize and move forward lead structures identified in its screens.

11. The lead optimization and pre-clinical activities supported by DTP should be available to both intramural and extramural researchers and should be utilized and prioritized based on the quality of the science and overall probability of success in generating a relevant therapeutic agent.

12. An NCI Office of HIV-AIDS Research should be established as an efficient mechanism for coordination of all NCI activities related to HIV-AIDS.

13. DTP should become a part of the Inter-Company Collaboration for AIDS Drug Development to share drug development information related to HIV/AIDS and to avoid duplication of efforts.

14. Given the extensive recommendations presented in this report, it would be appropriate for NCI to allocate resources to a level compatible with meeting the currently perceived needs for development of therapeutic agents for the treatment of AIDS.

Jack Edwards, chief of the Infectious Disease Division, University of California, Los Angeles, Harbor Medical Center, served as chairman of the review group.

Members of the review group were: Ronald Desrosiers, professor of microbiology and molecular genetics, Harvard Medical School; Daniel DiMaio, chairman, Department of Genetics, Yale University; Gregg Gonsalves, Treatment Action Group, New York City; Daria Hazuda, Merck Research Laboratories;

Elliott Kieff, professor of microbiology and molecular genetics and medicine, Harvard University; Martin Markowitz, assistant professor, Aaron Diamond AIDS Institute; David Matthews, senior director, head of crystallography, Agouron Pharmaceuticals Inc.; Donna Mildvan, chief, Infectious Diseases Division, Beth Israel Medical Center; William Powderly, director, AIDS Clinical Trials Unit, Washington University; Martin Rosenberg, senior vice president and director, Anti-Infectives Research, SmithKline Beecham; Richard Tidwell, professor of pathology, University of North Carolina at Chapel Hill; Leroy Townsend, professor of medicinal chemistry, University of Michigan; and Volker Vogt, professor of biochemistry, Cornell University.

*Science Policy:*

## Stem Cell Research Guidelines Formalize NIH Funding Policies

NIH this week published draft guidelines for government funding and oversight of research involving human pluripotent stem cells.

The guidelines largely formalize and clarify existing NIH policies of funding stem cell research, but not the derivation of stem cells from human embryos. Earlier this year, the National Bioethics Advisory Committee recommended that the government begin to fund the derivation of stem cells (**The Cancer Letter**, Sept. 17).

This cannot be done because every year since 1996, Congress amended the Labor-HHS appropriations bill to prohibit NIH funding of research "in which a human embryo [is] destroyed, discarded, or knowingly subjected to risk of injury greater than that allowed for research on fetuses in utero."

Anti-abortion activists are pushing legislation that would ban federal funding of stem cell research altogether.

NIH funds can be used to "support research to *derive* pluripotent stem cells from fetal tissue, as well as for research *utilizing* such cells," the guideline states. Though NIH has had the legal right to fund such work, it has not done so in the past, sources said.

The text of the draft guidelines is posted at http://www.nih.gov/news/stemcell/draftguidelines.htm

The document calls for establishing a committee to review documentation of compliance with the guidelines for stem cell research. According to the document, the committee, called Human Pluripotent Stem Cell Review Group, would "hold public review meetings when a funding request proposes the use of a newly derived line of human pluripotent stem cells that has not been reviewed previously by the HPSCRG in a public process or when an investigator proposes a protocol for the derivation of a new human pluripotent stem cell line from fetal tissue."

According to the document, NIH funds can be used to support pluripotent stem cell research from early human embryos "only if the cells were derived from early human embryos that were created for the purposes of infertility treatment and were in excess of clinical need of the individuals seeking such treatment."

Infertility clinics supplying the embryos would need to implement written policies and practices to ensure that no inducements are offered for donation of the embryos.

The guidelines state that protocols for donation of embryos are subject to approval by the Institutional Review Boards.

Applications for research involving stem cells will be reviewed for scientific merit by: 1) an initial review group, in the case of new or competing continuation applications; 2) by institute or center staff in the case of requests to use existing funds or applications for an administrative supplement; or 3) by the scientific drector in the case of intramural proposals prior to submission to the HPSCRG.

In addition to withholding support for the derivation of pluripotent stem cells, NIH will deny funding for the following forms of stem cell research:

—Research in which human pluripotent stem cells are utilized to create or contribute to a human embryo;

—Research in which human pluripotent stem cells are combined with an animal embryo;

—Research in which human pluripotent stem cells are used for reproductive cloning of a human;

—Research in which human pluripotent stem cells are derived using somatic cell nuclear transfer, i.e., the transfer of a human somatic cell nucleus into a human or animal egg;

—Research utilizing human pluripotent stem cells that were derived using somatic cell nuclear transfer, i.e., the transfer of a human somatic cell nucleus into a human or animal egg; and

—Research utilizing pluripotent stem cells that were derived from human embryos created for research purposes, rather than for infertility treatment.



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*Professional Societies:*

## AACI Moves To Pittsburgh, Elects New Board Members

The Association of American Cancer Institutes has established its administrative operations center at the University of Pittsburgh Cancer Institute.

AACI selected UPCI to manage its operations in response to a proposal submitted by Barbara Duffy Stewart, UPCI director of communications and public affairs. Stewart has been appointed the new executive director of the association. UPCI Director Ronald Herberman will serve as president of the association for the next two years.

Established in 1959, AACI is dedicated to multidisciplinary and inter-institutional collaborations on cancer through research, treatment, education and service programs. AACI accomplishes this through the large network of established cancer institutes across the country, which represent cancer constituencies from researchers, to physicians, to patients and patient advocates.

Over the next two years, Herberman plans to emphasize the role of cancer centers as leaders in providing access to the most advanced technology and most promising treatments. "It is at the nation's cancer centers where cures for cancer are being developed, and where patients can participate in the most up-to-date cutting-edge cancer therapies," Herberman said.

"Unfortunately, the majority of the public doesn't know this, because we haven't been very effective at promoting our centers' unique strengths and resources," Herberman said. "This should be a prime responsibility of the AACI, and I intend to make it a priority during my term."

Another objective of the association is to raise its visibility as a voice on national public policy issues related to cancer.

"The AACI represents the nation's most prestigious cancer centers and has enormous potential to play a pivotal role in maximizing government support for cancer research and in helping to craft legislation that removes barriers that have limited patient access to promising cancer therapies," Stewart said. "We look forward to developing the organizational capacity that the AACI will need to achieve recognition as a national leader and resource on cancer-related public policy issues."

In addition to Herberman, AACI elected the following officers at the annual meeting in September in Ann Arbor, MI: Max Wicha, University of Michigan Comprehensive Cancer Center, chairman; John Niederhuber, University of Wisconsin Comprehensive Cancer Center, vice president; and Jerome Yates, Roswell Park Cancer Institute, secretary-treasurer. Joining current AACI board members Franco Muggia, Kaplan Comprehensive Cancer Center; and Arthur Nienhuis, St. Jude Children's Research Hospital, are new board members: Paul Bunn, University of Colorado Cancer Center; Vincent DeVita, Yale Cancer Center; Marc Lippman, Lombardi Cancer Center; Robert Ozols, Fox Chase Cancer Center; William Peters, Barbara Ann Karmanos Cancer Institute; and Steven Rosen, Robert Lurie Comprehensive Cancer Center of Northwestern University.

For further information about AACI, contact Barbara Duffy Stewart, executive director, AACI Operations Center, phone 412-647-2076; fax 412-647-3659; e-mail stewartbd@msx.upmc.edu.

*National Academy of Science:*

## Report Calls For Major Change To Reduce Medical Errors

Reducing one of the nation's leading causes of death and injury—medical errors—will require rigorous changes throughout the health care system, including mandatory reporting requirements, according to a report from the Institute of Medicine of the National Academies.

The report lays out a comprehensive strategy for government, industry, consumers, and health providers to reduce medical errors, and it calls on Congress to create a national patient safety center to develop new tools and systems needed to address persistent problems.

The human cost of medical errors is high. Based on the findings of one major study, medical errors kill some 44,000 people in U.S. hospitals each year. Another study puts the number much higher, at 98,000. Even using the lower estimate, more people die from medical mistakes each year than from highway accidents, breast cancer, or AIDS.

While errors may be more easily detected in hospitals, they afflict every health care setting: day-surgery and outpatient clinics, retail pharmacies, nursing homes, as well as home care. Deaths from medication errors that take place both in and out of hospitals—more than 7,000 annually—exceed those from workplace injuries.

"These stunningly high rates of medical errors, resulting in deaths, permanent disability, and unnecessary suffering, are simply unacceptable in a medical system that promises first to 'do no harm,'" said William Richardson, chair of the committee that wrote the report and president and chief executive officer of the W.K. Kellogg Foundation. "Our recommendations are intended to encourage the health care system to take the actions necessary to improve safety. We must have a health care system that makes it easy to do things right and hard to do them wrong."

The committee sets as a minimum goal a 50 percent reduction in errors over the next five years.

The majority of medical errors do not result from individual recklessness, the report said, but from basic flaws in the way the health system is organized.

Stocking patient-care units in hospitals, for example, with certain full-strength drugs, even though they are toxic unless diluted, has resulted in deadly mistakes. Illegible writing in medical records has resulted in administration of a drug for which the patient has a known allergy. Medical knowledge and technology grow so rapidly that it is difficult for practitioners to keep up. The health care system itself is evolving so quickly that it often lacks coordination.

**Four-Part Plan**

The committee recommends a four-part plan designed to create both financial and regulatory incentives that will lead to a safer health care system:

—**A National Center for Patient Safety**. Congress should create a center for patient safety within the Department of Health and Human Services, the committee said. This center would set national safety goals, track progress in meeting them, and invest in research to learn more about preventing mistakes.

Administratively, the home for the center should be in the HHS Agency for Health Care Policy and Research; Congress would need to spend $30 million to $35 million to set it up, the committee said. Funding would need to grow to at least $100 million, a little more than 1 percent of the $8.8 billion spent each year as a result of medical errors that cause serious harm, the committee said.

—**Mandatory and Voluntary Reporting Systems**. The committee defines "error" as the failure to complete a planned action as intended or the use of a wrong plan to achieve an aim, and notes that not all errors result in harm. To learn about medical treatments that lead to serious injury or death and to prevent future occurrences, the committee recommends establishing a nationwide, mandatory public reporting system. Hospitals first, and eventually other places where patients get care, would be responsible for reporting such events to state governments. Currently, about a third of the states have their own mandatory reporting requirements.

The committee recommends federal legislation to protect the confidentiality of certain information. Specifically, data should be protected on medical mistakes that have no serious consequences, where the information is collected and analyzed solely for the purpose of improving safety and quality, the committee said.

—**Role of Consumers, Professionals, and Accreditation Groups**. Public and private purchasers of health care insurance must make safety a prime concern in their contracting decisions, the committee said. Licensing and certifying bodies should implement periodic re-examinations of doctors, nurses, and other key providers, based on both competence and knowledge of safety practices.

The Food and Drug Administration should increase its attention to public safety, the committee said. Efforts should be made to eliminate similar-sounding drug names as well as confusing labels and packaging that foster mistakes.

—**Building a Culture of Safety**. Health care organizations must create an environment in which safety will become a top priority, the committee said. This culture of safety means designing systems geared to preventing, detecting, and minimizing hazards and the likelihood of error, not attaching blame to individuals. The report stresses the need for leadership by executives and clinicians, and for accountability for patient safety by boards of trustees.

All hospitals and health care organizations should implement proven medication safety practices, such as using automated drug-ordering systems. the committee said. Patients themselves could provide a major safety check in most hospitals, clinics, and practices, by knowing which medications they are taking, the appearance, and the side effects, the committee said.

Copies of "To Err Is Human: Building a Safer Health System," are available from the National Academy Press, phone 202-334-3313 or 800-624-6242. The cost of the pre-publication report is $45 (prepaid) plus shipping charges of $4.50 for the first copy and $.95 for each additional copy.


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*Scientific Misconduct:*

## HHS To Change Role Of ORI In Response To Report

HHS has accepted the recommendations of a special review group on research misconduct and research integrity involving research funded by agencies of the U.S. Public Health Service.

Under the proposals agreed to by HHS Secretary Donna Shalala:

—HHS will adopt through rulemaking a new definition of research misconduct, which focuses on improper behaviors related specifically to the conduct of research. The definition was proposed by the National Science and Technology Council.

—Institutions that administer PHS-supported grants will maintain responsibility for conducting initial inquiries and investigations. When further fact finding is required by the federal government, it will be carried out by the HHS Office of Inspector General rather than the Office of Research Integrity, as has previously been the case.

—Inquiries and investigations into potential research misconduct will be separated from the decision making process of determining if misconduct occurred. The ORI will review institutional findings and will recommend actions and sanctions, when supported by findings, to the Assistant Secretary for Health, who will make the final decisions regarding misconduct, subject to appeal.

—The Departmental Appeals Board will continue to hear appeals from individuals who contest findings of misconduct. Each DAB appeals panel will include two scientists, and the appeals process will be streamlined with clarified procedures and rules for conducting hearings.

—Through ORI, HHS will require research institutions to provide training in the responsible conduct of research to all staff engaged in research or research training with PHS funds.

The report recommends clarifying and refining the definition of research misconduct by limiting misconduct to "fabrication, falsification, or plagiarism in proposing, performing or reviewing research, or in reporting research results."

ORI will continue to provide on-site technical assistance to institutional investigations where needed and oversight review of completed investigations. However, the review group recommended that the role of ORI be changed to emphasize preventing misconduct and promoting research integrity.

*Funding Opportunities:*

## RFA Available

**RFA OD-00-002: Clincal Research Curriculum Award**

Letter of Intent Receipt Date: March 24, 2000

Application Receipt Date: April 21, 2000

NIH invites educational and research institutions to apply for the new Clinical Research Curriculum Award (CRCA or K30). The program will be supported by all NIH Institutes and Centers.

The CRCA is an award to institutions and addresses, in part, the NIH initiative to improve the quality of training in clinical research.

NIH recognizes that highly trained clinical researchers are needed in order to capitalize on the many profound developments and discoveries in fundamental science and to translate them to clinical settings. The RFA is intended to stimulate the inclusion of high-quality, multidisciplinary didactic training as part of the career development of clinical investigators. The CRCA supports the development and/or improvement of core courses designed as in-depth instruction in the fundamental skills, methodology, theories, and conceptualizations necessary for the well- trained, independent, clinical researcher.

While many NIH programs support research experiences for new clinicians, not all of these trainees have the opportunity to receive formal course work in the design of clinical research projects, hypothesis development, biostatistics, epidemiology, disease mechanisms, medical technology, human genetics, and the legal, ethical and regulatory issues related to clinical research. This award is intended to support the development of new didactic programs in clinical research at institutions that do not currently offer such programs or, in institutions with existing didactic programs in clinical research, to support and expand their programs or to improve the quality of instruction. The goal of the program is to improve the training of the participants, so they can more effectively compete for research funding.

Clinical research includes: patient-oriented research, epidemiologic and behavioral studies, and outcomes or health services research. NIH defines patient-oriented research as research conducted with human subjects (or on material of human origin such as tissues, specimens, and cognitive phenomena) that requires direct interactions with human subjects.

Patient-oriented research includes the development of new technologies, understanding mechanisms of human disease, therapeutic interventions and clinical trials.

The mechanism of support for the RFA will be the K30 mechanism. The program award provides five years of support and is renewable.

A total budget for FY 2000 of approximately $4 million will be committed to fund applications submitted in response to the RFA. The maximum annual total cost per

award will be $200,000 in all years and approximately 20 awards will be made in FY 2000.

Inquiries: Belinda Seto, Office of Extramural Research, NIH, Bldg. 1, Room 252, Bethesda, MD 20892, phone 301-402-9128; fax 301-402-2642; e-mail bs11e@nih.gov

## ASBMT, Roche Offer Award For New Investigators

Application deadline: Jan. 14, 2000

American Society for Blood and Marrow Transplantation and Roche Laboratories invite applications for a $25,000 per year research award for new investigators. The award will be presented for the first time at the ASBMT 2000 annual meeting, March 29-April 1, in Anaheim, CA.

Applications that address prevention or treatment of graft-versus-host disease after transplant are of special interest. Applicants must be at the junior faculty level (instructor or assistant professor) and be an ASBMTmember or sponsored by a member.

Inquiries: ASBMT Executive Office, 85 W. Algonquin Rd., Suite 550, Arlington Heights, IL 60005; phone Alan Leahigh 847-427-0224; fax 847-427-9656; e-mail mail@asbmt.org

## NCI Contract Notice

The NCI Cancer Statistics Branch, Surveillance Research Program, in the Division of Cancer Control and Population Sciences, plans to negotiate with the Cherokee Nation, of Tahlequah, OK, for a contract for a two-year period to establish a cancer registry for the American Indians residing in the 14-county Cherokee Nation Tribal Jurisdictional Service Area who are eligible for health care through Tribal or Indian Health Service-operated health care facilities.

The goal of the project is the establishment of a population-based cancer registry, to be called the Cherokee Nation Cancer Registry, that will meet the standards of the NCI's Surveillance, Epidemiology and End Results Program in casefinding, patient follow-up, data processing, data reporting, and quality assurance by Dec. 31, 2001. At that time the contract may be extended to maintain the registry at SEER standards for an additional 19 months.

It is expected that the Cherokee Nation shall cost share for the establishment of the registry and assist in the development of agreements with the hospitals, clinics, pathology laboratories and other entities where data on American Indian cancer cases can be obtained.

*In Brief:*

## Porter's Press Secretary Moves To Academy Of Dermatology

(Continued from page 1)

**HARVEY GREENBERG**, Moffitt service chief of radiation oncology, was appointed medical director of physician affairs and will serve as vice-chairman for business affairs of the Interdisciplinary Oncology Program. . . . **DAVID KOHN** has been named associate executive director of communications by the American Academy of Dermatology effective January 2000. Kohn has been press secretary to **Rep. John Porter** (R-IL) since 1985 where, among his duties, he served as spokesman for the House Appropriations Subcommittee chaired by Porter, which has jurisdiction over the Department of Labor, Health and Human Services, and Education. . . . **LUTHER BRADY,** of Hahnemann Hospital, received the Philadelphia County Medical Society 1999 Strittmatter Award for achievement in the field of medicine Nov. 5. . . . **FREDRIC PRICE,** a University of Pittsburgh Medical Center-affiliated physician, was named national chairman of a committee studying the treatment of cervical cancer for the Society of Gynecological Oncologists. The committee will focus on developing an up-do-date set of practice guidelines for the treatment for gynecologic malignancies. Price and the committee will be reporting information on the standard treatment of cervical cancer through publications and Internet access on the SGO website: http://www.sgo.org. . . . **THE GROUP ROOM**, the nationally syndicated radio talk show about cancer, will present a live remote broadcast and town hall meeting on complementary aspects of cancer care, on Sunday, Dec. 12, 3-5 p.m. CT, from the University of Texas M.D. Anderson Cancer Center. Joining host **Selma Schimmel** will be **Judy Gerner**, administrative director of the "Place. . . of wellness" and director of Anderson Network Patient Services; and other experts from M.D. Anderson, including **Richard Theriault**, professor of breast medical oncology; **Lorenzo Cohen**, assistant professor of behavioral science; **Cindy Carmack,** a clinical psychologist; **Debra Sivesind**, a clinical nurse specialist and psychotherapist; and **Laura Baynham**, program coordinator of "Place . . . of wellness" and a professional counselor. To attend the live audience discussion phone 713-794-4700. To enter program discussions, phone 800-GRP-ROOM (800-477-7666).



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THE CANCER LETTER

Vol. 14 No. 11
November 1999

# Business & Regulatory Report

Formerly "Cancer Economics"

*Oncology Management:*

## OTN, CancerEducation.com In Alliance For Oncology Drugs And Information

**Oncology Therapeutics Network** of New York, a subsidiary of **Bristol-Myers Squibb** (NYSE:BMY), and **CancerEducation.com www.cancereducation.com** said they have formed a business alliance that will link their websites to provide medical professionals with the first fully-integrated, comprehensive on-line source for oncology pharmaceuticals, education, and information.

OTN said its oncology drug ordering system will be directly linked to the CancerEducation.com web site by oncology professionals for

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*Product Approvals & Applications:*

## FDA Approves Taxol For Node-Positive Breast Cancer After Doxorubicin Therapy

FDA approved the supplemental NDA for Taxol (paclitaxel) for sequential adjuvant treatment of node-posit ive breast cancer administered after a course of standard doxorubicin-containing combination chemotherapy. The drug is sponsored by **Bristol Myers-Squibb Co.**

The approval was based on a phase III intergroup study involving 3170 node-positive breast carcinoma patients who received adjuvant therapy with Taxol or no further chemotherapy after four courses of doxorubicin and cyclophosphamide. Patients who received four courses of Taxol once every three weeks had a 26-percent reduction in death and a 22-percent reduction in disease recurrence.

According to the FDA approval letter dated Oct. 25, results from the trial demonstrate "an overall favorable effect on disease-free and overall survival in the total population of patients with receptor-positive and receptor-negative tumors."

However, in unusual move, the agency included discussion of a retrospective subset analysis in the drug's label.

"In the clinical trial, there was an overall favorable effect on disease-free and overall survival in the total population of patients with receprorpositive and receptor-negative tumors, but the benefit has been specifically demonstrated by available data (median follow-up 30 months) only in patients with estrogen and progesterone receptor negative tumors," the agency said in a letter to BMS.

In the Clinical Studies section, the label states that "the beneficial effect of Taxol is clearly established in the receptor-negative subgroup

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## Two Firms To Offer Online Drug Ordering, Education

(Continued from page 1)

cancer-related educational presentations and extensive informational services. OTN will also become the CancerEducation.com oncology pharmaceutical ordering and distribution channel for office-based oncologists. The companies are exploring additional e-commerce opportunities for collaboration.

OTN said its online drug ordering service features secure 24 hour access to online ordering from the OTN catalog of products, pricing and product availability information and clinical information from the OTN Oncology Online Web site. Order forms are customized for each practice. Current invoices and credit memos and up-to-date reimbursement information are always available and the system is fully searchable for order, invoice and credit information in real time.

* * *

**US Oncology Inc.** (Nasdaq: USON) of Houston, earned $14.8 million ($0.15 per share) on revenues of $277.8 million for the third quarter ended Sept. 30. Merger-related costs reduced the company earning by $2.7 million, to 12.1 million.

Last year, the third quarter earnings of the two companies that formed U.S. Oncology were $15.0 million, and revenues $216.9 million.

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

**Business & Regulatory Report**

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

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

**Customer Service: 800-513-7042**
**PO Box 40724, Nashville TN 37204-0724**

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"We have yet to fully realize the benefits of the merger, and earnings per share for the third quarter were lower than expected," said R. Dale Ross, chairman of the board and CEO. "We experienced higher costs relating to drug management and did not achieve expected economies of scale. As we continue to integrate operations, we expect earnings per diluted share to remain stable for the fourth quarter of this year and to resume earnings growth in 2000. We remain confident in the strength of our business fundamentals and will continue to implement our strategic initiatives."

This is the first full quarter of integrated operations for the company, which was formed by the merger of American Oncology Resources Inc. and Physician Reliance Network Inc. last June.

The company provides cancer management services to over 800 affiliated oncologists in 26 states.

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**Pharmacia & Upjohn** (NYSE: PNU) of Peapack, NJ, said it has created a dedicated oncology business unit to expand its global cancer care franchise.

P&U said the move integrates its commercial oncology activities into a single reporting structure. "We are making cancer treatment a key driver of our growth," said CEO Fred Hassan. Jeff Buchalter has been appointed group vice president and head of the global oncology franchise and will report to Carrie Cox, senior vice president and head of global business management, the company said.

Earlier this year, P&U acquired **Sugen Inc**. which brought expertise in small molecule messaging that controls cancer and other diseases.

*Product Approvals & Applications:*

## In Unusual Move, FDA Includes Subset Analysis On Label

(Continued from page 1)

but that the benefit in receptor-positive patients is not yet clear."

The FDA Oncologic Drugs Advisory Committee decided the indication should include all node-positive patients, also noting the results of the subset analysis. Subset analyses are notoriously unreliable and are usually not accepted as evidence by FDA.

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**Genta Inc**. (Nasdaq: GNTA) of Lexington, MA, said FDA has granted Fast Track designation to bcl-2 antisense compound, G-3139, for use in combination

with dacarbazine for treatment of advanced malignant melanoma.

G3139 was designed to reduce the Bcl-2 protein level in cancer through an antisense mechanism that specifically targets the messenger-RNA produced by the bcl-2 gene, the company said.

In many human cancers, the Bcl-2 protein is believed to be a major factor in inhibiting apoptosis, or programmed cell death, and in contributing to resistance of those cancers to treatment with anticancer drugs.

Seven clinical trials are currently ongoing using G3139 by intravenous or subcutaneous route in patients with lymphoma and solid tumors, and additional clinical development is ongoing through a collaboration with NCI to study G3139 for small cell lung cancer, colorectal cancer and acute leukemia, the company said.

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**Nomos Corp**. of Sewickley, PA, said it has filed a 510-K application for FDA clearance to market Peregrine, a dose calculation system for which Nomos Corp. was granted an exclusive license by Lawrence Livermore National Laboratory last July.

Peregrine uses monte carlo statistical techniques to predict accurately the radiation dose to tumors and other structures within the patient's body during a radiation treatment. Current dose calculation methods approximate the radiation dose distribution in the patient based on dose distributions in water. With the refined Peregrine calculations, doctors and clinicians can improve the design of the treatment to concentrate curative radiation doses on tumors, with less damage to surrounding healthy tissue, the company said.

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**Rhone-Poulenc Rorer**, the pharmaceutical subsidiary of **Rhone-Poulenc S.A.** (NYSE: RP) of Collegeville, PA and Antony, France, said the Committee for Proprietary Medicinal Products of the European Union recommended approval of Taxotere (docetaxel) for the treatment of locally advanced or metastatic non-small-cell lung cancer after failure of prior chemotherapy.

The European Commission must endorse the CCPMP opinion before Taxotere receives final marketing authorization in this indication.

The CPMP opinion was based on the results of two phase III, multicenter studies involving patients with advanced non-smallcell lung cancer whose disease had progressed on prior chemotherapy.

In a phase III trial, 204 patients whose disease had failed to respond to platinum-based chemotherapy received either 75 mg/m$^2$ or 100 mg/m$^2$ of Taxotere given as a one-hour infusion on day one and repeated every three weeks, or best supportive care. BSC refers to measures aimed at maintaining patient comfort, including nutritional support and control of symptoms, such as nausea, vomiting, pain and shortness of breath.

In patients treated with Taxotere at 75 mg/m$^2$, overall survival (median is 9 months versus 4.6 months) and time to progression (median is 12.3 weeks versus 7 weeks) were significantly longer compared to patients receiving BSC. The one-year survival rate was also significantly longer in patients treated with Taxotere at 75 mg/m$^2$ (40 percent) versus BSC (16 percent).

Quality of life was assessed using several tools, including the Lung Cancer Symptom Scale and the European Organization for the Research and Treatment of Cancer QOL questionnaire. The analysis showed that patients treated with Taxotere used less radiotherapy and symptom-relieving medications and had less weight loss. The QOL evaluation also showed that patients treated with Taxotere had less pain and fatigue and more appetite.

In the second multicenter phase III trial, 373 patients with advanced NSCLC who were resistant to platinum-based chemotherapy received either treatment with Taxotere 75 mg/m$^2$ or 100 mg/m$^2$, every three weeks, or treatment with either vinorelbine, 30 mg/m$^2$ weekly, or ifosfamide, 2 gm/m$^2$ daily for three days every three weeks.

The study found that the one-year survival rate in patients treated with 75 mg/m$^2$ of Taxotere was 32 percent, compared to 19 percent in patients treated with either vinorelbine or ifosfamide.

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**Vical Inc**. (Nasdaq:VICL) of San Diego, said Allovectin-7 was granted the Ophan Drug designation for the treatment of invasive and metastatic melanoma.

Cancer centers throughout the U.S. are recruiting patients for phase III and phase II registration trials with Allovectin-7, the company said.

Allovectin-7, which uses a lipid-DNA complex to help the immune system recognize and attack cancer cells, is in phase II and phase III testing in certain patients with metastatic melanoma and in phase II testing in patients with unresectable head and neck cancer, the company said.

*Clinical Trials:*

## SWOG Begins Phase III Trial In Advanced Prostate Cancer

**Southwest Oncology Group** of San Antonio, TX, said it has begun the first phase III clinical trial to compare the chemotherapy combination of docetaxel (Taxotere) and estramustine phosphate (Emcyt) to the commonly used combination of mitoxantrone (Novantrone) and prednisone for the treatment of advanced, hormone-refractory prostate cancer.

Enrollment is underway and approximately 660 men are being recruited for the trial, which is being initiated by SWOG and funded by NCI in collaboration with the Cancer and Leukemia Group B.

Results of phase I/II studies have shown the combination of docetaxel and estramustine to be very active and well-tolerated in patients with hormone-refractory prostate cancer.

"The encouraging response rates seen thus far with the combination of docetaxel and estramustine provide hope that using a tolerable, more effective combination may prolong life in this group of difficult-to-treat patients," said SWOG study chairman Daniel Petrylak, assistant professor of medicine at Columbia College of Physicians and Surgeons, and director of the Genitourinary Oncology Program at Columbia Presbyterian Center of New York - Presbyterian Hospital, where this treatment regimen was developed and first studied.

SWOG said the primary objectives of the study are to determine if the docetaxel/estramustine combination improves overall survival and progression- free survival when compared to the mitoxantrone/prednisone combination and to compare toxicities related to the two treatments. Other objectives include assessments of the decline of prostate specific antigen levels and of quality-of-life between both treatment groups.

While prior clinical trials using single-agent chemotherapy have yielded objective response rates of 10 to 20 percent with subjective or stable response rates in another 20 to 40 percent of patients, no single agent or combination treatment has demonstrated a survival benefit for advanced, hormone-refractory prostate cancer patients in phase III trials.

The reported survival rate in these trials has been less than a year, ranging from five to 11 months, SWOG said. Palliative benefit can be achieved with the administration of mitoxantrone with corticosteroids, however, there is no evidence that survival is prolonged with this therapy.

Participants will be randomized at the SWOG coordinating center to receive one of two treatment regimens: oral estramustine taken three times daily for five days combined with intravenous docetaxel administered on the second day of treatment; or intravenous mitoxantrone administered every three weeks with twice daily oral prednisone taken for three consecutive weeks. A maximum of 12 cycles of either treatment regimen will be administered in the study.

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**Biogen Inc.** (Nasdaq: BGEN) of Cambridge, MA, said it has halted several trials of its anti-CD40 ligand monoclonal antibody compound until issues relating to thrombo-embolic events are completed.

The company said it was working with FDA on reviewing data and determining when trials could resume. Studies in Factor VIII inhibitor syndrome, islet cell transplantation and multiple sclerosis have been placed on hold. Patients already receiving the drug in the renal transplantation program will continue on therapy, and those patients who have benefited from therapy in the Immune Thrombocytopenic Purpura study can continue treatment. The company said it is discussing the continuation of the lupus trial with FDA.

"While these data are not clear yet, we are being very proactive because we are dealing with patients in these clinical trials who are at a substantially elevated risk for thrombo-embolic events," said Jim Vincent, Biogen CEO. "It is very complicated to determine whether the events that have been seen are connected to our drug or not. In the interests of patient safety, we have asked the investigators participating in the affected phase II trials to stop dosing patients at this time."

Humanized anti-CD40 ligand monoclonal antibody (hu5c8) is a novel immunomodulator that selectively binds to CD40 ligand, an important co-stimulatory molecule found on activated T cells, the company said.

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**NeoPharm Inc.** (AMEX: NEO) of Bannockburn, IL, said it has begun phase I trials of IL13 PE38QQR (IL13-toxin) for renal cell carcinoma.

Neopharm licensed IL13-toxin from FDA and the Center for Biologics Evaluation and Research in 1997. The first patient is currently under treatment at Providence Medical Center in Portland.

IL13-toxin is a targeted cytotoxin that uses the IL-13 receptor on the surface of cancer cells to deliver a bacterial toxin (PE38QQR), which has been shown to destroy tumor cells while sparing normal cell, the company said. IL13-toxin underwent pre-clinical testing in the laboratory of Raj Puri at CBER and at NeoPharm.

The company said a phase I trial will be conducted at the Lurie Cancer Center of Northwestern University in Chicago.

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**North American Scientific Inc**. (Nasdaq: NASI) of Chatsworth, CA and **Theseus Imaging Corp**. said Theseus has begun a clinical trial of its Apomate Kit for the preparation of Technetium Tc-99m recombinant human Annexin V for imaging apoptosis in tumors before and after anti-cancer treatment.

The study will enroll patients with non-small cell lung cancer, disseminated breast cancer and non-Hodgkins lymphoma.

In initial studies, Apomate uptake was seen in some patient lung tumors within 24-48 hours after treatment, the company said. The current study will correlate the tumor uptake of the imaging agent with its response to treatment, the company said. Greater uptake of the agent—reflecting cellular apoptosis—is expected to correlate to greater degree of tumor cell death.

NAS said Apomate imaging is intended to provide physicians with information about individual patient response to specific anti-tumor drugs within hours of starting treatment. Preliminary animal studies have shown that Tc-99m Annexin V, a normally occurring human protein, localized within a few hours of treatment on tumor cells that responded to treatment. On the other hand, Tc-99m Annexin V did not localize at animal tumors that did not respond to anti-tumor treatment, the company said.

The current trial will study the effectiveness of Apomate imaging in identifying patients whose tumors are likely to respond to the specific anti-tumor treatment selected by their physician as well as identifying patients whose tumors are unlikely to respond to the specific anti-tumor medicine selected.

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**Procept Inc.** (Nasdaq: PRCT) of Cambridge, MA said it has begun a phase II trial of its O6-Benzylguanine hemosensitizing agent in combination with the chemotherapeutic drug carmustine for the treatment of multiple myeloma at the Ireland Cancer Center at University Hospitals of Cleveland and Case Western Reserve University under the direction of Stanton Gerson.

The study is one of several phase II clinical trials that will be sponsored by NCI in various cancer indications including colon cancer, glioma, melanoma, and sarcomas. The trials will be conducted in accordance with a cooperative research and development agreement signed with NCI in 1998, the company said.

BG is a chemosensitizer designed to overcome tumor resistance to a significant class of commonly used chemotherapeutic agents known as O6-alkylating agents. BCNU and temozolomide are members of this class. BG inactivates tumor AGT, a DNA repair protein which interferes with the effectiveness of these agents.

Inactivation of AGT in cells derived from 11 human tumor types, including multiple myeloma, rendered these cells more sensitive to the cytotoxic effects of several alkylating agents, the company said. In preclinical animal studies, treatment with BG increased the anti-tumor activity of BCNU in brain, colon, and prostate cancers and of temozolomide in glioma and melanoma, the company said. Published human clinical data show that a correlation exists between low levels of AGT and survival in brain tumor patients treated with BCNU chemotherapy.

*Emerging Technologies:*

## WSU Investigator Isolates New Class Of Taxol Genes

**Cytoclonal Pharmaceutics Inc.** (Nasdaq: CYPH, CYPHW, CYPHZ) of Dallas, said Rodney Croteau of Washington State University and under contract to Cytoclonal, has isolated a new class of Taxol genes.

The isolation of the new genes, as well as the discovery of previous Taxol genes proprietary to Cytoclonal, make up part of the program with Bristol-Myers Squibb to generate an optimized production system for Taxol using fermentation and genetic engineering, the company said.

The new class of genes code for Cytochrome P450 Oxygenases. Which are involved in the pathway used for the synthesis of paclitaxel, the active ingredient in Taxol. A patent for one of the most important first steps involving Taxadiene Synthase has been issued and patent protection for the new genes is pending., the company said.

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**Myriad Genetics Inc.** (Nasdaq: MYGN) of Salt Lake City, said it has introduced a new rapid-turnaround service for breast and ovarian cancer susceptibility testing. Rapid BRACAnalysis is used in patients recently diagnosed with breast cancer. The service can produce results in 7 days following receipt of the specimen at Myriad, the company said.

To achieve these faster timeframes, a special parallel process is used that includes running each Rapid BRACAnalysis specimen in duplicate through the test procedure. A dedicated technician manages the specimen to eliminate potential processing delays. The standard BRACAnalysis service costs $2,400, which is reimbursed by insurance. There is a supplementary charge of $1,100 for the Rapid BRACAnalysis service.

Over 390 health care insurers pay for BRACAnalysis, and more than 94 percent of patients seeking insurance reimbursement are successful, the company said.

*Deals & Collaborations:*

## Firm To Collaborate With MGH To Develop Detection Device

**Advanced Research Technologies Inc**. of Montreal, said it has signed an agreement with **Massachusetts General Hospital** to develop a laser-based optical detection system for breast cancer.

Under the three-year agreement, the collaborators said they intend to develop a relatively inexpensive device that will complement existing systems used to diagnose breast cancer. The device will provide a better lesion detection rate among women undergoing routine mammography. The agreement also gives ART the right to obtain an option to market such a device under conditions determined between MGH and ART.

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**AltaRex Corp**. (Toronto: AXO) of Waltham, MA, said it has made operational changes designed to development and commercialization OvaRex MAb for the treatment of ovarian cancer. The company said it will suspend its product development activities for products other than OvaRex MAb and will reduce staff and facility related costs. The current clinical trials of OvaRex MAb will continue on track and the company will continue to seek a commercialization partner.

"AltaRex's focus has always been to develop novel antibody-based therapeutics for a number of deadly cancers. At this time, the company believes that advancing OvaRex MAb through development to the market is in the best interests of its shareholders and ovarian cancer patients," said Richard Bagley president and CEO of AltaRex Corp. "We are very appreciative of the contributions that all the employees have made to help apply AltaRex's Anti-idiotype Induction Therapy technology platform to the development of cancer products."

As part of the operational change, associated product support areas are being reduced by approximately 15 positions. Staff and operations that are required for the continuation of the clinical trials for OvaRex MAb will remain. Prior to the reduction, AltaRex employed 39 individuals.

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**American Pharmaceutical Partners Inc.** of Schaumburg, IL, said it will market the first generic Cisplatin.

APP has been granted a 180-day exclusivity to market generic Cisplatin against Platinol-AQ (Cisplatin for injection) sold by **Bristol-Myers Squibb**. According to industry reports, U.S. sales of Platinol-AQ injection in 1998 were approximately $100 million out of a total $450 million in sales of platinum-based oncology products.

The U.S. District Court for the District of New Jersey ruled last week that a patent held by Research Corp. Technologies and Bristol-Myers Squibb for Cisplatin Injection is invalid, thus clearing the way for APP's launch. Together with three other companies, APP said it had challenged the Cisplatin patent, which was to expire in 2012. Because APP was the first company to challenge the patent, it was granted the 180-day right of exclusivity.

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**Axys Pharmaceuticals Inc**. (Nasdaq: AXPH) of South San Francisco and **Signal Pharmaceuticals Inc**. of San Diego, said Signal has granted to Axys exclusive, worldwide development and marketing rights to for the Signal selective estrogen receptor-beta modulators for the treatment of cancer.

The SERM-beta compounds licensed from Signal under this agreement are novel small molecules that modulate the activity of the beta subtype of the estrogen receptor found on breast, uterine and a number of other cancer cells, the company said The closely related alpha subtype of the estrogen receptor is the target of two widely prescribed drugs, tamoxifen

and raloxifene for treatment of cancer and osteoporosis respectively, the companies said.

The worldwide license granted to Axys provides access to all of Signal's SERM-beta drug discovery technology and ER-beta selective compounds used for the treatment or prevention of cancer., the company said. Signal will retain rights for all indications outside of oncology under the terms of the collaborative agreement. Axys will provide payments to Signal in the form of a license fee, research funding, research milestones and royalties. Signal may exercise a profit share option in the U.S. at a predetermined point during development in lieu of royalties on product sales. Signal would share equally in the profits in the U.S. on product sales by Axys by paying an equal share of the remaining development and commercialization costs in the U.S., the companies said.

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**Duke University Health System** of Durham, NC, and **DuPont Pharmaceuticals Co**. said they had entered into an agreement under which Duke will license to DuPont patent rights on novel anti-estrogen compounds that may be active in treating breast cancer, including tamoxifen-resistant breast cancer.

DuPont said it will conduct pre-clinical and clinical development, marketing and worldwide sales of anti-cancer compounds.

Duke said the agreement is the fourth in a series of actions recently taken by DuPont to enhance its pharmaceuticals business through alliances and acquisitions.

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**ImmunoGen Inc.** (Nasdaq: IMGN) of Norwood, MA, said it has purchased an option from **Duke University** and **Johns Hopkins University** to license a cancer-targeting antibody, co-developed by investigators at the two institutions, for use with its Tumor-Activated Prodrug technology.

The antibody, which targets a tumor-associated variant of the Epidermal Growth Factor receptor, has demonstrated the ability to bind tightly to the variant EGF receptor on the surface of a wide variety of human tumor cells, the company said. Under the terms of the agreement, ImmunoGen will evaluate the applicability of the antibody to deliver ImmunoGen's DM1 cytotoxic agent specifically to cancer cells.

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**Nen Life Science Products** of Boston, said it has entered into a three-year cooperative research and development agreement with NIH to improve the sensitivity of gene expression profiling techniques.

Nen and the Cancer Genetics Branch of the NIH National Human Genome Research Institute will use patented Nen signal amplification technology to reduce the amount of total RNA required for accurate gene expression profiling experiments by as much as 200 times.

If successful, the work will vastly improve the effectiveness of microarray-based assays for many applications, the company said.

A key element of the project is the Nen Tyramide Signal Amplification technology. TSA, patented under the name CARD (Catalyzed Reporter Deposition), is already widely used to increase the sensitivity of in situ hybridization protocols. Nen has filed a patent for a method to use TSA in gene expression profiling, to reduce total RNA sample requirements from typical levels of 50 to 200 micrograms per assay, down to one to two micrograms. The CRADA seeks to reduce the requirement further, to less than one microgram, the company said

"At that level, it will be possible to apply microarray assay methods to human biopsy and tissue samples from mice, which cannot be done using 's technology," said Russell Garlick, vice president for research and development at Nen and principal investigator for the project, titled, "Improved Gene Expression Profiling Using Catalyzed Reporter Deposition Tyramide Signal Amplification Methods."

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**NewBiotics Inc**. of San Diego, said it has contracted with **ILEX Oncology Services Inc**., a subsidiary of **ILEX Oncology Inc.** (Nasdaq: ILXO), for pre-clinical development of the NewBiotics lead compound, NB1011, for the treatment of drug resistant colon cancer.

"Because NB1011 works by a novel mechanism of action, exploiting a well defined difference between normal and malignant cells, it offers a unique opportunity to benefit patients, said Dennis Slamon, professor and chief of hematology and oncology at University of California at Los Angeles. Slamon sits on the Scientific Advisory Board at NewBiotics.

The NB1011 compound is part of the core ECTA technology for targeted cancer and anti-infective drug discovery. NewBiotics said the technology may enhance the beneficial effects of antibiotic therapy or chemotherapy while minimizing damage done to healthy cells.

The company said it has identified one of the key resistance mechanisms blocking the full therapeutic effects of commonly used chemotherapeutics like fluoropyrimidines, Tomudex and doxorubicin. The NewBiotics ECTA technology uses the resistance mechanism to generate antitumor compounds inside the cancer cell. The company said it plans to begin clinical trials in about 12 months.

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**Onyx Pharmaceuticals Inc**. (Nasdaq: ONXX) of Richmond, CA, said it has signed a collaboration agreement with **Warner-Lambert Company** (NYSE: WLA) to develop and commercialize the Onyx phase III anticancer product, ONYX-015, as well as two new armed anticancer viruses.

Onyx and WL will co-promote ONYX-015 and the two new products in the U.S. and Canada, and will share equally in profits.

Onyx said WL will make an upfront payment and equity investment in Onyx totaling $15 million. $40 million in funding will go for the phase III clinical trials and other ongoing clinical development studies for ONYX-015. WL will support research and development of two new products. Over $100 million additional funds could be payable to Onyx on the achievement of milestones for the products. The clinical development costs of the products will be shared 75 percent by WL and 25 percent by Onyx, once WL has funded ONYX-015.

ONYX-015 is a genetically modified adenovirus that has been shown in preclinical and clinical studies to replicate in and kill tumor cells deficient in p53 tumor suppressor gene activity. Onyx and WL are preparing to initiate a pivotal phase III clinical trial of ONYX-015 in the fourth quarter of 1999 or early in 2000 that combines the virus with chemotherapy as a treatment for patients with recurrent head and neck cancer, the company said. ONYX-015 is also in phase II clinical trials for patients with colorectal cancer that has metastasized to the liver and for patients with pancreatic cancer, the companies said.

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**Pharmacia & Upjohn** (NYSE: PNU) of Peapack, NJ said it has received FDA approval for Aromasin (exemestane tablets) for breast cancer in postmenopausal women.

Aromasin is the first aromatase inactivator for use in advanced breast cancer in patients whose tumors stop responding to tamoxifen therapy, the company said. The most common drug-related adverse events were hot flashes, nausea, fatigue, increased sweating, and increased appetite. Aromasin was generally well-tolerated in clinical trials, the company said.

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**Photogen Technologies Inc.** (OTC BB: PHGN) of Knoxville, TN said it has formed a joint venture with **Elan Corp. plc** (NYSE: ELN) of Dublin, Ireland, to develop and commercialize nanoparticulate diagnostic imaging agents for the detection and treatment of cancer that has spread to the lymph nodes.

Photogen Technologies said the companies want to develop a treatment that would reduce by more than 50 percent the number of lymph node surgeries. This reduction would be achieved by precisely locating the nodes where cancer has spread and at the same time, if necessary, treating the affected lymph nodes in one all-inclusive, non-invasive procedure.

"This corporate venture with Elan in the field of lymphography will enable us to redouble our efforts in bringing to market non-invasive methods for determining how much cancer a patient has and how far it has spread," said John Smolik, president and CEO of Photogen. "With our approach, we believe we can significantly reduce the number of lymph node surgeries used to determine the spread of cancers, including melanoma and cancers of the breast, prostate, lung, and head and neck."

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**UroCor Inc.** (Nasdaq: UCOR) of Oklahoma City, said it has signed a marketing agreement with **Prostate Services of America**, a marketer of medical equipment and services for prostate therapy, to sell ProstaSeed I-125 sources to PSA customers.

UroCor said the implants, called "seeds," will be a valuable addition to its line of products and services used for the diagnosis, prognosis, and treatment of prostate cancer.

Approximately 200,000 new cases of prostate cancer are diagnosed in the U.S. each year, and about 60 percent of these are potentially treatable with brachytherapy, the company said..

UroCor said it had entered into an agreement last September, with **Mallinckrodt Inc**., (NYSE: MKG). Mallinckrodt said the agreement states that it will market ProstaSeed through its 35 nuclear pharmacies and the 80 independent pharmacies that it services. UroCor previously received marketing approval for ProstaSeed from FDA and anticipates receiving clearance from the Nuclear Regulatory Agency shortly, the company said.

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