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# With NIH "Accountability" As Background, Advocates Support Budget Increases

As Congress continues to speed toward doubling of the NIH budget between 1998 and 2003, advocates of these steep increases are confronting an increasingly powerful chorus of voices calling for "accountability" on the part of NIH for its new funds.

So far this year, the call for keeping NIH accountable has come primarily from the House Committee on Science, but it is certain to resonate in the appropriations committees and among some patient groups.

The word "accountability" is being applied to Centers for Disease Control and Prevention as well, as supporters of the Atlanta-based agency

(Continued to page 2)

*In Brief:*

## Hong Succeeds Curran As AACR President, Horwitz Is President-Elect; 5 New Directors

NEW ORLEANS—**Waun Ki Hong** became president of the American Association for Cancer Research at the association's annual meeting in New Orleans on March 26. **Susan Band Horwitz** became president-elect and **Tom Curran** became past president.

Hong is professor and chairman, American Cancer Society Clinical Research Professor, Charles A. LeMaistre Distinguished Chair in Thoracic Oncology, Department of Thoracic/Head and Neck Medical Oncology, and chief of cancer medicine, University of Texas M. D. Anderson Cancer Center.

Hong has been a member of the Board of Directors and served as chairman of the 2000 Annual Meeting Program Committee. He also has been a member of the Task Force on Clinical Investigations, International Affairs Committee, Special Conferences Committee, Task Force on Clinical Investigations, and the Committee on By-Laws Revisions.

Hong has also been involved in organizing committees of the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, AACR/Japanese Cancer Association Meeting, and Joint Conference of the AACR/International Agency for Research of Cancer. He is the deputy editor and senior editor for clinical trials and chemoprevention of the AACR journal, Clinical Cancer Research, and has served on the Editorial Board of Cancer Research and of Cancer Epidemiology, Biomarkers & Prevention.

Horwitz is the Falkenstein Professor of Cancer Research and co-chairman, Department of Molecular Pharmacology, Albert Einstein College

(Continued to page 8)

# NIH Advocates Addressing Calls For Accountability

(Continued from page 1)

are trying to justify a large increase for its cancer programs. CDC's supporters include the American Cancer Society and an umbrella group called One Voice Against Cancer. Also, the CDC agenda is likely to emerge through the National Dialogue on Cancer and the National Cancer Legislation Advisory Committee. Both initiatives were launched and funded by ACS.

Moreover, advocates of funding increases for NIH are facing competition from proponents of increases for research agencies that did not do as well in recent years and are likely to do even worse under the Bush Administration. These include the National Science Foundation, the Department of Energy, and the National Aeronautics and Space Administration. Ironically, at some point, this competition may turn into an alliance, based on increasing dependence of life sciences on physics and engineering research, some players note.

Looking beyond the doubling, the NIH institutes' constituencies will have to devise a strategy for fiscal 2004, the year after the doubling is achieved. The Administration's budget proposal indicates that starting that year, NIH would receive "stable, moderate funding increases." After years of growth open the horizons of research, a return to moderate increases would have a devastating effect, observers say.

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**NCCR Testimony**

Testifying before the House Labor, HHS and Education Appropriations Subcommittee, the National Coalition for Cancer Research asked for at least a 16.5 percent increase for NIH, an increment needed to stay on course toward the doubling. The coalition also supports the $5.1 billion contained in NCI's Bypass Budget, said Donald Coffey, NCCR president.

"We are truly at a critical juncture in cancer research," Coffey said. "The recent publication of the draft map of the sequence of all of the genes in human DNA—an incredible public-private venture—represents tremendous opportunities for researchers to move closer to the detection, prevention, diagnosis, and treatment of cancer."

NCI clinical trials program is not keeping up with the pace of development of new agents, Coffey said. "The NCI's bypass budget for FY 2002 addresses the important issue of increasing patient and physician participation in clinical trials," Coffey said. "It also calls for increasing the development and testing of promising new agents in clinical trials."

Coffey also urged that the government continue to fund research involving human pluripotent stem cells. "The NCCR supports the guidelines NIH put in place last summer governing embryonic stem cell research, and we urge Congress and the Administration to retain these guidelines, which include a number of stringent ethical safeguards to ensure the appropriate use of research funds," he said.

**FASEB and AAMC**

The testimony of the Federation of the American Societies of Experimental Biology cautioned against slowing down the pace of investment in biomedical research.

"The sequencing of the human genome, along with the completion of other animal and plant genomes, is radically enhancing what we know about human health and illness," FASEB President Mary Hendrix said to the appropriations subcommittee.

"This new knowledge will inaugurate a new era in the diagnosis and treatment of disease," said Hendrix, a basic researcher and deputy director of the Holden Comprehensive Cancer Center at the University of Iowa in Iowa City. "These opportunities—the result of decades of investment in basic research—will improve the quality of life and dramatically reduce human suffering on a global scale. We urge our nation's leaders to maintain the course they have charted and continue the expansion of our

research capacity."

FASEB recommendations include:

—An appropriation of $23.7 billion in fiscal 2002. This will sustain the momentum—begun in fiscal 1999—toward the national goal of doubling the NIH budget. The new money should fund investigator-initiated grants.

—That NIH implement new and strengthen existing opportunities for funding of new investigators.

—Instituting a substantial increase in the base salaries of NRSA-funded post-doctoral fellows and benefits comparable to those received by permanent employees.

—Full funding of administrative costs associated with increased regulation, such as for human subjects protection and animal care by the agencies funding research.

The Association of American Medical Colleges called for enhancement of translational research. "Recent increases in the NIH's overall budget have allowed the agency to support early translational research on new molecular entities and new therapeutic strategies of great promise, but which is still too uncertain to attract significant investment from industry," Terrance Cooper, professor of microbiology and immunology at the University of Tennessee and chairman of the AAMC Council of Academic Societies, said in testimony before the appropriations subcommittee.

"The AAMC supports additional funding for the continued expansion of clinical research and clinical research training opportunities, including rigorous, targeted post-doctoral training; developmental support for new and junior investigators; career support for established clinical investigators, especially to enable them to mentor new investigators; and funding the recent expansion of the clinical research loan repayment program to the extramural community," Cooper said.

Cooper said changes in health care delivery systems threaten the clinical research infrastructure at medical schools and teaching hospitals. "The AAMC supports an additional $500 million for the NIH National Center for Research Resources," he said.

**The CDC Agenda**

In its submitted testimony, the American Cancer Society supported the NIH doubling goal and Bypass Budget funding fro NCI. However, the society also called for scaling up public health interventions by CDC.

"ACS strongly believes that increased cancer research funding at NIH and NCI should not come at the expense of vital cancer prevention and control programs at CDC," said the society in its submitted testimony. "Effective interventions exist today that will help cancer patients, survivors and their families. As the nation's leading prevention agency, CDC plays an important role in translating what is learned from research into information that can be delivered to people in their communities—especially ensuring that those populations disproportionately burdened by cancer receive the benefits of our investment in cancer research."

One Voice Against Cancer, a coalition of about 40 public health organizations that advances goals that appear to coincide with those of ACS, recommended an appropriation of $315 million for the following programs at CDC:

—$55 million for the National Cancer Registries Program ($18.6 million increase). The program coordinates state-based data collection.

—$10 million for the Comprehensive Cancer Control Initiative ($6.9 million increase). The program works toward an integrated and coordinated approach to reduce the incidence, morbidity and mortality of cancer through prevention, early detection, treatment, rehabilitation, and palliation. According to One Voice testimony, additional funding would allow CDC to continue and expand its initiatives in comprehensive control through state and community efforts. Particular attention should be paid to raising public awareness and enhancing professional education on cancers not currently addressed by CDC programs, including hematological, genitourinary, and digestive system cancers, the document states.

—$25 million for Colorectal Cancer Screening, education and outreach ($16.1 million increase).

—A minimum of $210 million for the National Breast and Cervical Cancer Early Detection Program ($36.1 million increase). "With additional funding, the NBCCDEP can ensure that many more of this nation's low-income, medically-underserved and high-risk women are screened for breast and cervical cancer," the document states.

—$15 million for the Prostate Cancer Awareness Campaign ($3.8 million increase).

Last year, the campaign to secure a dramatic funding increase for CDC ran into opposition from some advocacy groups. Critics challenged the agency to explain how it spends its funds and justify potential increases. This year, One Voice, a group that advocates

for the Atlanta agency, apparently borrowed the critics' call for "accountability."

"One Voice Against Cancer insists that federal dollars designated for cancer programs be well-spent," the group said in its submitted testimony. "One Voice Against Cancer has established its own working group to develop a process to monitor how agencies spend these program monies and to work to improve effective and efficient programmatic use of funding. We believe that our work in this area will complement the work of Congress, the NIH, the NCI and the CDC—and be of benefit, most of all, to the persons and families affected by cancer."

**Patient Groups Call for Finetuning PRGs**

Testifying before the subcommittee, the North American Brain Tumor Coalition called for greater collaboration between NCI and the National Institute of Neurological Disorders and Stroke. The two institutes recently formulated a Progress Review Group report on brain tumors.

Lawrence Pizzi, executive director of the coalition, suggested the following areas of collaboration:

—The two institutes should strengthen mechanisms for coordination and collaboration among extramural researchers.

—NINDS, NCI, and the Center for Scientific Review should coordinate review of brain tumor research proposals. Coordination of the referral, review, and funding of brain tumor research proposals by NINDS, NCI, and CSR would facilitate implementation of the brain tumor research plan developed by the BT-PRG.

—The recently-established NCI-NINDS Neuro-oncology Branch should develop a strategic plan and budget for its ongoing collaborative ventures and take responsibility for facilitating further interaction between NINDS and NCI. The coalition recommended that the branch consider its role in training of brain tumor researchers who can conduct translational research.

—NCI and advocacy organizations should cooperate in the education of brain tumor patients and physicians regarding brain tumor treatment options. Educational programs of patient organizations may be more effective if coordinated with educational initiatives supported by NCI.

The coalition also proposed that advocates begin a dialogue with NCI and the brain tumor clinical consortia related to the development and evaluation of new treatments. Such communication would ensure the involvement of advocates in the development of appropriate and meaningful clinical endpoints, the coalition said.

Testifying for the Lymphoma Research Foundation of America, cancer survivor Jerry Crum said a PRG alone would not be enough. "One purpose of the PRG is to identify the overlaps in research and where gaps exist," said Crum, a participant in the PRG on lymphoma, leukemia, and myeloma being developed by NCI. "The PRG report is designed to create a national prioritized research agenda for lymphoma and other hematological cancers. But we believe that the recommendations alone will not bring about needed change rapidly enough.

"Therefore, we request that a budget plan accompany the report," Crum said.

The group also requested that the National Institute on Environmental Health Sciences report to Congress on the state of its research portfolio on lymphoma and hematological cancers and CDC to expand its support for investigating the possible environmental causes of lymphoma and increase data collection on the disease.

The National Prostate Cancer Coalition is asking for $135 million for the peer reviewed research program at the Department of Defense, and "sufficient funding" for the intramural program at Walter Reed Army Hospital. The current DOD prostate cancer program has $100 million.

The National Breast Cancer Coalition is asking for $175 million—level funding—for the DOD peer-reviewed breast cancer program.

"What you have done is set in motion an innovative and highly efficient approach to fighting the breast cancer epidemic," Maria Carolina Hinestrosa, member of Programa Nueva Vida and a member of the NBCC board of directors, said in testimony before the DOD appropriations subcommittee. "What you must do now is continue to support this effort by funding research that will help us win this very real and devastating war against a cruel enemy."

*Tobacco Policy:*

## Stronger Anti-Smoking Efforts Needed For Women, SG Says

Women account for 39 percent of all smoking-related deaths each year in the U.S., a proportion that has more than doubled since 1965, according to a report on women and smoking released this week by

Surgeon General David Satcher.

The report concludes that the increased likelihood of lung cancer, cardiovascular disease, and reproductive health problems among female smokers makes tobacco use a serious women's health issue.

Increased marketing by tobacco companies has stalled progress in smoking cessation by women, and recent increases in smoking among teenage girls threaten to wipe out any progress that has been made in the last few decades, Satcher said.

"In the early decades smoking prevalence was more prominent among men, and it took nearly 25 years before the gap narrowed and smoking became commonplace among women," Satcher said. "Women not only share the same health risk as men, but are also faced with health consequences that are unique to women, including pregnancy complications, problems with menstrual function, and cervical cancer."

The report, "Women and Smoking: A Report of the Surgeon General," summarizes patterns of tobacco use among women, factors associated with starting and continuing to smoke, the health consequences of smoking, tobacco marketing targeted at women, and cessation and prevention interventions.

"Smoking is a critical women's health issue that must be addressed on all fronts," HHS Secretary Tommy Thompson said. "We must begin this battle in schools before girls even begin to smoke, and we must share with teenage girls that smoking is not only harmful, but it is not glamorous. Society must not glorify smoking."

"In addition, we must provide information to women and minority groups detailing the harmful affects of smoking as well as the benefits of smoking cessation," Thompson said. "The facts are clear: smoking significantly reduces life expectancy and hampers quality of life."

Since 1980, nearly three million U.S. women have died prematurely from smoking. The new report calls for stronger national and local efforts, particularly from women's groups, to push for the implementation of proven solutions to reduce and prevent tobacco use among women and girls.

The report calls for increasing public awareness of the devastating impact of smoking on women's health; exposing and countering the tobacco industry's targeting of women; encouraging public health policymakers, educators, medical professionals, and women's organizations to work for policies and programs that deglamorize and discourage tobacco use; reducing disparities related to tobacco use and its health effects among different ethnic/racial populations; decreasing nonsmokers' exposure to environmental tobacco smoke; and mounting comprehensive statewide tobacco control programs proven to be effective in reducing and preventing tobacco use.

Developed by HHS' Centers for Disease Control and Prevention to document the impact of smoking on women's health in the U.S., the report also provides analyses of the global impact of smoking on women.

"We estimate that smoking prevalence among women varies markedly worldwide from as low as 7 percent in developing countries to 24 percent in developed countries," CDC Director Dr. Jeffrey Koplan said. "The rise in smoking among women around the world has coincided with aggressive Western-style tobacco advertising. One of the most common themes used in developing countries is that smoking is both a passport to and a symbol of a woman's emancipation, independence, and success."

"We have firm evidence of a direct association between tobacco marketing and smoking prevalence," Koplan said. "Earlier this month, the Federal Trade Commission reported that cigarette companies spent $8.24 billion on advertising and promotions in 1999 in the U.S., a 22.3 percent increase from the $6.73 billion spent in 1998. Fortunately, we have proven science-based evidence that counter-marketing strategies can be a powerful tool to change social norms. The CDC is committed to working globally to create a broad framework to curb the global epidemic of tobacco-related disease, particularly as it relates to women and young people."

The report outlines solutions for preventing and reducing smoking among women, including:

—Encouraging quitting for women of all ages.

—Implementing science-based smoking cessation interventions into widespread clinical practice. This action would be as cost-effective as other medical interventions such as mammography and treatment of high blood pressure, the report said.

—Enacting comprehensive statewide tobacco control programs. Results from states such as Arizona, California, Florida, Maine, Massachusetts, and Oregon show that science-based tobacco control programs have successfully reduced smoking rates among women and girls. California is starting to observe the dramatic public health benefits of its sustained efforts. Between 1988 and 1997, the incidence rate of lung cancer among women declined by 4.8 percent in

California but increased by 13.2 percent in other regions of the U.S.

—Encouraging a more vocal constituency on issues related to women and smoking. Concerted efforts are needed from women's and girls' organizations, women's magazines, public health policymakers, medical groups, and volunteer organizations to call public attention to lung cancer and other smoking-related diseases among women, and to call for policies and programs that deglamorize and discourage tobacco use.

"Despite the overwhelming evidence of effective tobacco use intervention strategies, we clearly have a long way to go to meet our public health objectives of cutting smoking in half among women and girls," Satcher said. "We know more than enough to prevent and reduce tobacco use. Now we must commit the attention and resources to translate this knowledge into action to save women's lives."

The report is available on the CDC's Web site at http://www.cdc.gov/tobacco. Copies of the Executive Summary and the report's "At A Glance" can also be ordered via fax by calling 800-CDC-1311 or by writing the CDC's Office on Smoking and Health, Mail Stop K-50, 4770 Buford Highway, Atlanta, Ga. 30341.

A consumer section on quitting smoking is available on the National Women's Health Information Center Web site, http://www.4woman.gov, sponsored by the HHS Office on Women's Health.

*NCI Programs:*

## Meharry, Vanderbilt Win Grant For Research Collaboration

NCI has awarded $7.5 million to support expansion of a partnership between Meharry Medical College and the Vanderbilt-Ingram Cancer Center.

The partnership is designed to combine the strengths of the historically black academic health center and the NCI-designated comprehensive cancer center, located only two miles apart.

For Meharry, the collaboration is expected to enhance and stabilize its ability to conduct competitive cancer research.

For Vanderbilt-Ingram, the relationship helps overcome challenges in its ability to develop and sustain research into racial and ethnic disparities in cancer incidence, mortality and morbidity.

"It is taking Meharry, an institution with real strength in working with patients in this community, and the research excellence of Vanderbilt-Ingram and putting them together," said George Hill, vice president for sponsored research at Meharry.

The majority of the funding over a five-year period will go directly to Meharry—approximately $1.3 million each year. The remaining $200,000 per year will go to Vanderbilt-Ingram.

The partnership includes research collaboration, joint recruitment and joint appointment of scientists and clinicians, development of shared research resources at Meharry, funding of pilot research projects, and training opportunities to encourage and prepare minorities to enter careers in cancer care or research.

"Three things make this partnership particularly strong," said Harold Moses, director of the Vanderbilt-Ingram Cancer Center and co-principal investigator in the project. "First and foremost, we have developed a real trust and respect between the two institutions. Second, our geographic proximity. And third, the Meharry-Vanderbilt Alliance has built a strong foundation. Many important issues were already worked out through that process."

The partnership is coordinated through the Alliance, formed to promote interaction between Meharry and Vanderbilt Medical Center to enhance educational, research and clinical programs at and between both institutions.

"The idea behind this grant is to create a real and enduring partnership between these institutions, to address the racial disparities in cancer," said Samuel Evans Adunyah, chairman of Biochemistry at Meharry and co-principal investigator. "We not only have done that, but we are leading the way. The feedback we have received from the NCI indicates that we can be an important role model for others in the country who want to form similar collaborations."

The Meharry/Vanderbilt-Ingram partnership was launched about a year ago with $1 million in supplemental support to Vanderbilt-Ingram's cancer center core grant, which covers administrative costs of operating an NCI-designated cancer center. The teams then put in place programs and plans to compete for the Cancer Research Partnership Grant. This grant is designed to help reduce racial disparities in cancer by supporting collaboration between historically minority institutions and established NCI-designated cancer centers.

In addition to supporting graduate training of minority scientists with an interest in cancer research, the partnership also continues development of the infrastructure need to conduct clinical trials at Meharry.

*Funding Opportunities:*

# RFA Available

**RFA-HS-01-005: The Effect of Health Care Working Conditions on Quality of Care**

Letter of Intent Receipt Date: April 20, 2001

Application Receipt Date: May 21, 2001

Agency for Healthcare Research and Quality is seeking applications for research grants intended to identify, characterize, and directly measure the effect of the health care work environment on the safety and quality of care provided by health care workers. Support will be through the R01 mechanism.

Inquiries: Kelly Morgan, program analyst, Center for Primary Care Research, Agency for Healthcare Research and Quality, 6010 Executive Blvd, Suite 201, Rockville, MD 20852, phone 301-594-1782; fax 301-594-3721; e-mail kmorgan@ahrq.gov

# Program Announcements

**PA: Models for HIV Disease and AIDS-Related Malignancies (Reissued)**

This NCI initiative encourages investigator-initiated grant applications to develop predictive biochemical, cellular, in vivo and mathematical models for the evaluation of new therapies against HIV disease and AIDS-related malignancies. Exploratory basic research studies on the mechanism of action of HIV genes, cellular genes involved in HIV gene replication, and gene products are excluded from this PA.

Inquiries: Kenneth Cremer, Biological Carcinogenesis Branch, Division of Cancer Biology, NCI, phone 301-496-6085; e-mail kc47i@nih.gov or cremerk@mail.nih.gov

**PAR-01-074: NCI Transition Career Development Award for Underrepresented Minorities**

NCI's Comprehensive Minority Biomedical Branch invites transition career development award applications for protected time in which to develop and receive support for an initial cancer research program from the mentored to the independent stage. Support will be provided through the NIH K22 award mechanism.

Inquiries: Sanya Springfield, chief, Comprehensive Minority Biomedical Branch, NCI, 6116 Executive Blvd, Suite 7018A, Bethesda, MD 20892-7405, Rockville, MD 20852, phone 301-496-7344; fax 301-402-4551; e-mail ss165I@nih.gov

# RFPs Available

**Visible Human Project Anatomical Issues**

National Library of Medicine, in partnership with National Institute of Dental and Craniofacial Research, National Eye Institute, National Institute of Deafness and Other Communication Disorders, NCI, National Institute of Mental Health, National Institute of Neurological Disorders and Stroke, and National Science Foundation seeks proposals for the award of one or more completion type, cost reimbursement contracts to rectify anatomic methodology issues cited as negative outcomes from anatomic observations of the Visible Human Project. The project will involve the development of a VHP sequential standard method to address and solve the anatomic methodology issues, and develop tissue enhancements or markers for neurovascular structure identification.

Inquiries: Daniel Hartinger, contracting officer, Office of Acquisitions Management, National Library of Medicine, 8600 Rockville Pike, Bldg 38A/B1N17, Bethesda, Maryland 20894, phone 301-496-6546; fax 301-402-0642; e-mail dh29a@nih.gov

**Identification of Single Nucleotide Polymorphisms in Disease Susceptibility Genes**

National Institute of Environmental Health Sciences is soliciting offers for a contract to: establish a catalog of SNPs in environmental response genes based on direct re-sequencing of selected genes and use high-throughput sequencing technologies utilizing a national sample repository for analysis of sequence variation in the US population and to make this data available to the scientific community via centralized public databases. The estimated level of effort is for the base contract is 35,760 labor hours and 119,200 for all options. Estimated period of performance is 3 years for the base contract and 4 years if all options are exercised. The electronic version of the RFP will be available on the Internet at: http://www.niehs.nih.gov/dert/rcb/rfp.htm.

Inquiries: National Institute of Environmental Health Sciences, Marilyn Whaley, contracting officer Research Contracts Branch, DERT, 79 T.W. Alexander Dr, 4401 Bldg, P. O. Box 12874, Research Triangle Park, NC 27709; phone 919-541-0416; fax 919-541-2712; e-mail whaley@niehs.nih.gov). Requests should reference RFP NIH-ES-01-07.

**Studies to Evaluate the Toxicology and Carcinogenic Potential of Selected Chemical in Laboratory Animals for the National Toxicology Program:** Cresol, 1,2-Dibromo-2,4-Dicyanobutane, Tetrachloroazobenzene, Ginseng, and Kava Kava Extract

NIEHS is soliciting offers for a contract to evaluate the toxicologic and carcinogenic potential of selected chemicals via dosed feed, dermal, or gavage routes of administration. The principal investigator, toxicologist, chemist, veterinarian, health and safety officer and quality assurance unit officer shall be employees of the contract laboratory. Estimated level of effort is 1,505 labor hours for the base contract and 116,160 labor hours for all options. Inquiries: See preceding Notice. Requests should reference RFP NIH-ES-01-08.

*In Brief:*

## Bush Nominates VA Official For HHS Deputy Secretary

(Continued from page 1)

of Medicine. She also is associate director for drug development at the Albert Einstein Comprehensive Cancer Center. Horwitz has been a member of the AACR Board of Directors and has served on numerous AACR committees. She is a former recipient of the AACR-Cain Memorial Award.

Curran, member and chairman, Department of Developmental Neurobiology, St. Jude Children's Research Hospital, completed his one-year term. He has been a member of the AACR board since 1998.

AACR also announced the election of five new board members: **Ronald DePinho, Tyler Jacks, Frederick Appelbaum, George Vande Woude,** and **Barbara Weber**. They will serve three-year terms.

DePinho is professor of medicine, American Cancer Society Research Professor, director, Transgenic Mouse Program, Harvard Medical School.

Jacks is associate investigator, Howard Hughes Medical Institute, and professor of biology, Massachusetts Institute of Technology, Center for Cancer Research.

Appelbaum is senior vice president and director, Clinical Research Division, Fred Hutchinson Cancer Research Center, head, Clinical Transplant Research Program.

Vande Woude is director, Van Andel Research Institute, Grand Rapids, MI.

Weber is professor of medicine and genetics, University of Pennsylvania School of Medicine; director, Cancer Genomics Program, Abramson Family Cancer Research Institute.

* * *

**PRESIDENT BUSH** nominated Virginia Secretary of Health and Human Resources **Claude Allen** as deputy secretary of the U.S. Department of Health and Human Services. Allen has served in the administration of Virginia **Gov. Jim Gilmore** since January 1998. He was responsible for overseeing 13 agencies and 15,000 employees. Allen led Gilmore's initiative for a Virginia Patients Bill of Rights that passed in 1999, giving patients the right to appeal adverse coverage decisions made by their health plan and receive direct access to physician specialists. Allen was counsel to the Virginia attorney general and, later, deputy attorney general for the Civil Litigation Division in the attorney general's office. . . . **JOHNS HOPKINS** Oncology Center received a gift of $2.2 million from the Avon Products Foundation, from funds raised by the Avon Breast Cancer Crusade. The gift will support several novel approaches to managing breast cancer from molecular genetic biomarkers to behavioral aspects of women in following screening recommendations, as well as the development of new programs that reach out to underserved populations, said **Nancy Davidson**, the Johns Hopkins Breast Cancer Research Professor and director of the breast cancer program. Other participants in the Avon-supported studies include **Kathy Helzlsouer, Sara Sukumar, Deborah Armstrong, Allan Hess, Ann Klassen**, and **Dmitri Artemov**. The gift to Hopkins is part of a $16.2 million total that Avon has awarded to breast cancer programs at Harvard Comprehensive Cancer Center/Massachusetts General Hospital; University of California, San Francisco; Northwestern University/Robert H. Lurie Comprehensive Cancer Center; University of Alabama at Birmingham Comprehensive Cancer Center; University of California at Irvine Chao Family Comprehensive Cancer Center; Cancer Care, Inc.; Boston Medical Center; Olive View and the Iris Cantor Center for Breast Imaging at UCLA Medical Center; Howard University Cancer Center; and, Food & Friends, of Washington, DC. . . . **RICHARD O'REILLY**, chairman of pediatrics and chief of the Bone Marrow Transplantation Service at Memorial Sloan-Kettering Cancer Center, took office as president of the American Society for Blood and Marrow Transplantation earlier this month at the society's annual meeting in Keystone, CO. **Joseph Antin**, associate professor of medicine at Harvard Medical School, is the newly elected vice president, to become president in 2003. **Daniel Weisdorf**, University of Minnesota, took office as secretary. Three new directors are: **Andrew Pecora**, Hackensack University Medical Center; **Catherine Verfaillie**, University of Minnesota; and **Edward Ball**, University of California, San Diego. **John Wingard**, director of the Bone Marrow Transplant Program at University of Florida College of Medicine, was elevated to president-elect and will become president in 2002. . . . **AMY LANGER**, executive director of the National Alliance of Breast Cancer Organizations, has won the Society of Surgical Oncology's James Ewing Layman Award. The award is presented annually to a non-physician who has made a significant contribution to improving the care of cancer patients. Langer received the award March 18 at the society's annual cancer symposium, in Washington.

THE CANCER LETTER

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# Business & Regulatory Report

*Product Approvals & Applications:*

## FDA Says Bristol's UFT "Not Approvable" For Colorectal Cancer, Contrary To ODAC

**Bristol-Myers Squibb Co.** (NYSE: BMY) of Princeton, NJ, said it received a "not approvable" letter from FDA on UFT capsules plus leucovorin calcium tablets for the treatment of advanced colorectal cancer.

The agency's decision disregards a unanimous recommendation of the Oncologic Drugs Advisory Committee to approve the drug. The application was presented to ODAC in September 1999. The agency's handling of the UFT application has generated interest on Capitol Hill and was the subject of a series of stories in **The Cancer Letter.**

(Continued to page 2)

*Oncology Management:*

## US Oncology Renegotiates Agreements To Operate Under Net Earnings Model

**US Oncology Inc.** (Nasdaq: USON) of Houston said it has renegotiated affiliation agreements with Rocky Mountain Cancer Centers of Denver, Kansas City Oncology, Hematology Group of Kansas City, MO, and Birmingham Hematology and Oncology of Birmingham, AL, to operate under net earnings agreements.

Under the net earnings model, US Oncology and affiliated practices participate proportionally in practice revenue and operating costs. The alignment of interests through the use of this model will result in a more predictable financial performance.

"The modification of these agreements provides the platform for US Oncology to begin to satisfy the need in outpatient cancer centers and PET installations in the local cancer community," said Dale Ross, chairman and CEO of US Oncology.

The company's revenues for the year ended Dec. 31, 2000, increased 21% to $1.3 billion from $1.1 billion in the same period last year. Net loss, including all one-time charges, totaled $72.6 million, or $(0.72) per share, compared to net income of $48.2 million, or $0.47 per diluted share last year.

The one-time charges included $138 million, about 25 percent of the company's intangible assets, related to the projected financial impact of converting the remaining practices under the net revenue model, the company said. USON also established a $32 million reserve related to planned costs for closing operations in some markets.

(Continued to page 3)





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## Bristol-Myers "Disappointed" By FDA Decision On UFT

(Continued from page 1)

"We are very disappointed by this decision from the FDA," Peter Ringrose, president of Bristol-Myers Squibb Pharmaceutical Research Institute, said in a statement. "We remain committed to developing UFT around the world to its fullest potential and will consider all available options to obtain approval of UFT in the U. S."

More than 500,000 patients worldwide have been prescribed UFT, an oral equivalent of 5-FU, for a variety of diseases, including colorectal, gastric, lung and breast cancers, the company said.

* * *

**Matrix Pharmaceutical Inc**. (Nasdaq: MATX) of Fremont, CA, said FDA has accepted its new drug application for IntraDose Injectable Gel for refractory or recurrent head and neck cancer.

IntraDose delivers high concentrations of cisplatin for an extended time period at the injection site while reducing systemic effects associated with intravenous administration, the company said.

"We will continue to work closely with the agency to facilitate the review process," said Michael Casey, president, CEO and chairman of Matrix.

* * *

**NeoPharm Inc**. (Nasdaq: NEOL) of Lake Forest, IL, said it has reached an agreement with FDA to expand until 2003 the existing cooperative research and development agreement of IL13-PE38 for tumors that express IL-13 receptors.

NeoPharm said it has increased the scope and funding of the CRADA. Phase I trials of the agent are being conducted in both systemic kidney cancer and intratumoral brain tumor administration, the company said.

* * *

**Novartis Oncology** of East Hanover, NJ, said it has submitted marketing authorization applications globally for Glivec (formerly STI571) for chronic myeloid leukemia in the blast crisis, accelerated phase or in chronic phase after failure of interferon-alpha therapy.

Submissions were made in the U.S. and the European Union, and the filing for Switzerland, Japan and other countries is expected soon, the company said.

FDA has designated the therapy fast track status, the company said.

Glivec, a signal transduction inhibitor, molecularly targets an abnormal protein produced by the specific chromosomal abnormality called the Philadelphia chromosome, which is present in CML.

The filing is based on study results from approximately 1,230 patients in 32 centers located in five countries, the company said. To date, the therapy has been studied in more than 5,000 patients in 30 countries.

"Glivec marks the beginning of a new stage in cancer therapeutics development," said David Parkinson, vice president, clinical research, Novartis Oncology. "By understanding the molecular abnormality causing the cancer—CML in this case—we can design drugs that target the fundamental biochemical abnormalities associated with cancers, with better treatment results and fewer toxic effects on normal cells."

The filing is supported by data from three phase II studies, whose endpoints included both hematologic and cytogenetic response rates, the company said.

"The development of the drug has been a tremendous experience for the investigator community," said Brian Druker, professor of medicine, Oregon Health Sciences University and principal investigator for the phase I CML study. "The drug has offered us not just an opportunity to provide a drug to patients that has truly changed the course of their lives, but has allowed us to evaluate a drug that may be the first of many that may radically change

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how cancer is treated."

In clinical trials, Glivec has been generally well tolerated, with side effects including nausea, muscle cramps, edemas, skin rash, diarrhea, heartburn, and headache, which have been largely mild or moderate in intensity, the company said.

Fewer than three percent of patients have experienced serious side effects such as the potential for liver toxicity, fluid retention syndrome, and hemorrhages.

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**Ribozyme Pharmaceuticals Inc.** (Nasdaq: RZYM) of Boulder, CO, said it has submitted an investigational new drug application to the Canadian Therapeutics Products Programme to begin clinical trials with Herzyme, for breast and ovarian cancer.

The ribozyme is designed to downregulate the HER2/neu oncogene, the company said.

Medizyme Pharmaceuticals Ltd., an RPI joint venture with an affiliate of **Elan Corp. plc**, is developing Herzyme the company said.

The HER2/neu gene is overexpressed in about 25-30 percent of all breast cancers and is associated with progression of the disease, the company said. Herzyme has shown in vitro preclinical effectiveness in reducing HER2/neu expression.

Phase I trials will be conducted at the British Columbia Cancer Agency hospital in Vancouver, Canada, under the direction of Karen Gelmon, the company said. The trials will assess the safety, tolerability and pharmacokinetics of Herzyme when given as a single, daily subcutaneous injection.

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**SkyePharma Plc** (Nasdaq: SKYE; London: SKP) of London and its marketing partner **Chiron Corp.** (Nasdaq: CHIR) of Emeryville, CA, said they have received clearance from FDA to return the DepoCyt cytarabine liposome injection to the market for lymphomatous meningitis.

Chiron and SkyePharma said they voluntarily withdrew DepoCyt in October 1999 because it was discovered that certain batches did not meet regulatory specifications. There were no adverse events attributed to the recalled batches, the companies said.

DepoCyt is an injectable, sustained-release formulation of the chemotherapeutic agent, cytarabine, the companies said.

Using the SkyePharma proprietary lipid-based drug delivery technology, DepoFoam, DepoCyt gradually releases cytarabine into the cerebral spinal fluid and extends the dosing interval to once every two weeks as compared to the standard intrathecal chemotherapy dosing of two times per week.

A controlled, open-label, multi-center study showed that treatment with formulation resulted in a 41 percent response rate versus a 6 percent response rate with standard cytarabine, the companies said.

The most documented side effect from DepoCyt was arachnoiditis, an inflammation of the covering of the brain and spinal cord that causes symptoms such as headache, nausea, vomiting and fever, the companies said. Arachnoiditis was generally transient and reversible, the company said.

*Oncology Management:*

## Medicare To Expand Benefits For Colorectal Screening

(Continued from page 1)

With one-time charges excluded, net income was $47.6 million ( $0.47 per diluted share), compared to $59.4 million ($0.59 per diluted share) in the same period last year.

* * *

**Medicare** said it would expand colorectal screening exam benefits beginning July 2001, to include a screening colonoscopy.

Medicare guidelines, issued because of congressional legislation that was amended at the end of 2000, include: fecal occult blood tests, reimbursable annually for all patients; flexible sigmoidoscopy, reimbursable once every four years for average-risk patients; screening colonoscopy, reimbursable once every 10 years for average-risk patients; and a screening colonoscopy, reimbursable once every two years for high-risk patients.

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Cancer program development and implementation consultants **CDP Services Inc.** and **Cancer CarePoint Inc.** of Atlanta announced their recent merger.

The staff of the new company, **Oncology Solutions LLC,** will include C.D. "Dunk" Pruett, David Fulcher, Richard Taylor, and Rhonda Mealor are the principals of the new consulting firm. Senior officers of the new firm include Vice Presidents Chad Schaeffer and Kelley Simpson.

"This represents an outstanding opportunity to bring a group of truly experienced cancer program consultants together and provide an even higher level of service to our institutional and physician clients," said Richard Taylor.

*Clinical Trials:*

## Firm Begins Phase II Trial Of LDP-341 For Myeloma

**Millennium Pharmaceuticals Inc.** (Nasdaq: MLNM) of Cambridge, MA, said it has begun a phase II trial of LDP-341, formerly PS-341, for multiple myeloma.

LDP-341 is an investigational proteasome inhibitor for a variety of cancers, including hematologic malignancies and solid tumors, the company said.

The multi-center trial is an open label study of LDP-341 alone, or in combination with dexamethasone, a chemotherapeutic agent, to determine its safety and efficacy, the company said. A second randomized, open-label study of two doses of LDP-341 in patients who have failed to respond to, or relapsed, following front-line therapy, is scheduled in the second quarter of 2001, the company said.

"Millennium will initiate a series of phase I/II and phase II trials to explore the safety and efficacy of LDP-341 in additional oncology indications in solid tumors as well as hematological malignancies as both a single agent and in combination with other chemotherapeutic agents," said Lee Brettman, senior vice president, clinical development and medical affairs at Millennium.

"There is a tremendous need for new treatment options for multiple myeloma," said Kenneth Anderson, director of the Jerome Lipper Multiple Myeloma Center at Dana-Farber Cancer Institute, investigator in the LDP-341 trial, assistant to Millennium with the trial design and supervisor of patient dosing at the Dana-Farber/Partners Cancer Care trial site. "LDP-341, with its unique mechanism of action as a proteasome inhibitor, represents a promising new therapeutic approach in hematologic malignances, and we are very encouraged by its potential application in multiple myeloma."

**In another development,** Millennium and Protein Design Labs Inc. (Nasdaq: PDLI) of Freemont, MA, said they have agreed for Millennium to have rights to multiple humanized antibodies under the PDL antibody humanization patents.

Under the terms of the agreement, PDL would receive an undisclosed up-front signing fee and royalties on net sales of any resulting antibody products, the companies said.

Millennium said it could acquire commercial product licenses for up to three humanized antibodies from PDL within a five-year option period, which could be extended for an additional two-years.

Millennium said it would be responsible for product development, manufacturing and marketing of any resulting antibody products. Specific financial terms of the agreement were not disclosed.

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**OSI Pharmaceuticals Inc.** (Nasdaq: OSIP) of Uniondale, NY, said it has begun the first in a series of phase 1b trials to determine the safety, tolerance, pharmacokinetics and preliminary anti-cancer activity of escalating doses of OSI-774 in combination with docetaxel and other chemotherapy agents for advanced cancer.

The first open label, non-randomized study will be a collaboration among Eric Rowinsky, director of clinical research, Institute of Drug Development in San Antonio, Manuel Hidalgo, of the University of Texas Health Science Center also in San Antonio and Manuel Valdivieso, of the University of Texas Southwestern Medical Center in Dallas, the company said.

OSI-774 is a small-molecule, anti-EGFR drug candidate that has demonstrated anti-cancer activity in single agent, open label phase II studies in non-small cell lung, head and neck and ovarian cancers, the company said.

The studies form part of a comprehensive global development plan by OSI with its alliance partners **Genentech Inc**. and **Roche**, the company said. The plan encompasses the phase 1b program, additional phase II trials, and phase III studies directed toward registration of OSI-774 in both refractory and front-line treatment indications.

"The combination study of OSI-774 with Taxotere represents the first of ten clinical trials that the OSI/Genentech/Roche alliance anticipates this year," said Colin Goddard, chairman and CEO of OSI.

Taxotere is approved for locally advanced or metastatic non-small cell lung or breast cancer after failure of prior platinum-based chemotherapy, the company said.

Studies conducted in NSCLC, head and neck and ovarian cancers, that examined the use of OSI-774 as a single agent in advanced, refractory patients have demonstrated a well tolerated safety profile and anti-cancer activity, the company said.

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**Applied Molecular Evolution Inc.** (Nasdaq: AMEV) of San Diego said it has begun a phase I trial

with the second generation of Vitaxin, a monoclonal antibody humanized and optimized by **Applied Molecular Evolution Inc.** and licensed to **MedImmune Inc.** (Nasdaq: MEDI).

Vitaxin, an angiogenesis inhibitor, is the first of a second-generation biotherapeutic to enter clinical trials after optimization through directed evolution, a process for optimizing genes and proteins for specific commercial purposes, the company said.

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**BresaGen Ltd.** (Nasdaq: BSGNY; ASX: BGN) of Athens, GA, said it has begun a phase II study of E21R for chronic myelomonocytic leukemia.

The trial is being conducted at four sites in Australia, the company said.

A phase I study of the compound showed it to be well tolerated over a 10-day course of treatment with none of the toxic side effects associated with existing treatments for leukemia, the company said.

The drug acts on leukemic cells through two mechanisms: first, by inhibiting growth of the leukemic cells and second, by induction of cell death," said John Smeaton, president and CEO of BresaGen.

Under the agreement signed last December 2000, **British Biotech plc** (Nasdaq: BBIOY; LSE: BBG) has been granted an exclusive worldwide license to commercialize E21R for all indications and will carry out the clinical studies for regulato approval, the company said.

British Biotech would pay BresaGen equity, cash and conditional milestone payments of $8 million for the development of E21R, with further conditional milestone payments of up to $6 million on the successful development for any non-leukemic indications, the company said.

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**Cell Genesys Inc.** (Nasdaq: CEGE) of Foster City, CA, said it has begun a phase I/II trial of GVAX, a vaccine for multiple myeloma..

The trial, conducted by Ivan Borrello and Hyam Levitsky of Johns Hopkins Oncology Center, will evaluate the safety and efficacy of the vaccine in combination with bone marrow transplantation in advanced myeloma, the company said.

Preclinical studies demonstrated prevented relapse of leukemia and increased the overall survival of the treated animals, the company said.

GVAX cancer vaccines are comprised of tumor cells that have been irradiated and genetically modified to secrete granulocyte-macrophage colony stimulating factor, a hormone that plays a key role in stimulating the immune response to vaccines.

"We are optimistic the vaccine will be an important complement to the current standard of care for hematologic malignancies such as multiple myeloma and leukemia," said Joseph Vallner, executive vice president and chief operating officer of Cell Genesys.

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**Introgen Therapeutics Inc.** (Nasdaq: INGN) of Austin, TX, said it has begun phase I trials of INGN 241, adenoviral-mda7, for solid tumors.

Elizabeth Grimm, Ashbel Smith Professor, Departments of Tumor Biology and Surgical Oncology, M. D. Anderson Cancer Center is th The principal investigator is e principal investigator, the company said.

In the preclinical study, the agent caused growth arrest and induced apoptotic death in melanoma cells from both early and metastatic stages of disease, the company said. The anti-tumor effects were tumor-selective, as INGN 241 did not kill normal melanocytes. melanoma "Gene therapy for using a gene originally isolated from growth- arrested melanoma cells may provide a unique approach," said Grimm. "Adenoviral mda-7 is a broad spectrum anti-cancer agent and uses growth control mechanisms that are different than other gene therapy approaches."

The melanoma differentiation associated gene-7 (mda-7) was discovered by Paul Fisher of Columbia University, who identified in preclinical studies that mda-7 is up-regulated during melanoma differentiation, the company said.

* * *

**Protarga Inc.**, a Conshohocken, PA, based privately held company, said it has begun phase II studies of Taxoprexin DHA-paclitaxel.

Separate clinical studies for eight types of cancer are being conducted at 20 hospitals in the U.S. and the U.K, the company said. The first phase II patient received treatment for non-small cell lung cancer earlier this month under the direction of Paul Ellis at Guy's Hospital in London.

The study would valuate the effectiveness and safety of the compound in up to 400 cancer patients, the company said. Concurrent clinical studies are being conducted for cancers of the breast, colon/rectum, kidney, lung, pancreas, prostate, skin and stomach. Protarga said it has also started studies of the investigational drug in combination with certain anticancer therapies. The first of these combination studies, Taxoprexin DHA-paclitaxel with carboplatin,

began recently under the direction of Stanley Kaye, Cancer Research Campaign Professor of Medical Oncology, at The Royal Marsden Hospital in London. The principal investigator is Christopher Twelves of the CC Department of Medical Oncology, University of Glasgow, the company said.

In the NSCLC study, Taxoprexin treatment will be the first chemotherapy the lung cancer patients receive for their advanced disease, the company said. David Dunlop of the St. Mungo Institute, North Glasgow University Hospitals NHS Trust, is the prinicpal investigator.

A member in the class of taxane drugs, DHA-paclitaxel is a synthetic small molecule made by chemically linking paclitaxel, the active ingredient in Taxol to the natural fatty acid docosahexaenoic acid, an approved nutritional additive, the company thought.

"By attaching a small fatty acid molecule to paclitaxel, we improve delivery to tumor cells and its duration of action," said Forrest Anthony, vice president of clinical development at Protarga.

DHA-paclitaxel has also been designed to improve the safety of taxane therapy, the company said. The compound is only activated when the chemical bond between the DHA and paclitaxel is subsequently cleaved. The first phase I clinical study, conducted by Ross Donehower and Antonio Wolff at the Johns Hopkins Oncology Center, demonstrated that 4.6 times more taxane can be safely administered relative to the current maximum FDA-approved Taxol dose. None of the phase I patients experienced hair loss or significant nerve problems, nausea or vomiting, which are frequent side effects following Taxol administration, the company said.

*Deals & Collaborations:*

## Faulding, NaPro In Agreement For Marketing Paclitaxel

**Faulding Pharmaceuticals**, a division of F H Faulding & Co. Ltd. of Adelaide, South Australia, and **NaPro Biotherapeutics Inc.**, (Nasdaq: NPRO) of Boulder, CO, entered into a marketing and sales agreement with for paclitaxel, the companies said.

Under the agreement, NaPro said it would supply paclitaxel raw material exclusively to Faulding to formulate and marketed and sold by Faulding in Europe. Faulding said it would pay an upfront licensing fee $7.5 million and share equally in the net sales of the product in the new territories.

Paclitaxel sales in Europe were estimated at $330 million ending December 2000, the company said.

**In a related development**, NaPro and Abbott Laboratories (NYSE: ABT) of Abbott Part, IL, recently filed an abbreviated new drug application FDA for paclitaxel in the U.S.

"Submitting the ANDA is a major milestone in our plan to expand our presence in the oncology market," said Christopher Begley, senior vice president, hospital products, at Abbott.

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**Abbott** said it has acquired the U.S. **BASF** pharmaceutical business, which includes the global operations of **Knoll**, for $6.9 billion in cash.

"The acquisition enables us to broaden our global pharmaceutical infrastructure, acquire late-stage and marketed products, increase our pharmaceutical research and development spending and access leading monoclonal antibody technologies," said Miles White, chairman and CEO of Abbott.

"The pharmaceutical business complements the product and development portfolio in several of our core franchises, including cancer, cardiovascular, neuroscience/pain and metabolic diseases," said Jeffrey Leiden, executive vice president, pharmaceuticals and chief scientific officer.

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**Applied Genomic Technology Capital Funds** of Cambridge, MA, said it has closed on capital commitments of $150 million for its first venture funds.

AGTC Funds said it would focus on early- stage companies developing applications of genomic discoveries, information, and technologies. Founded by NewcoGen Group and OneLiberty Ventures, both of Cambridge, MA, the funds would leverage expertise in venture creation and venture capital investing, and tap the opportunities of the human genome project.

AGTC Funds limited partners include both institutional investors and corporations with an interest in genomics, the company said. Corporate sponsors include Affymetrix, Compaq Computer Corp. and Millennium Pharmaceuticals. Institutional investors in the funds include Hillman Company, OneLiberty Ventures and Paine Webber Group Inc.

"Publication of the human genome sequence intensifies a world-wide race to develop genomic applications," said Noubar Afeyan, managing partner of AGTC Funds. "The combination of open source codes and genomic tools will enable new applications in many industries, including health care, agriculture, materials, nanotechnology, energy, environmental and

computing."

AGTC Funds has made four investments to date: AnVil Informatics, a data mining and visualization services and software developer for genomics-driven research; Genomics Collaborative, developer of a Global Repository of DNA and tissue samples for gene discovery; Hypnion, a gene and drug discovery company developing treatments for sleep disorders and Nanostream, developer of microfluidic components and systems for life sciences research, clinical diagnostics and other applications.

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**Atrix Laboratories Inc.** (Nasdaq: ATRX) of Fort Collins, CO, said **Transmucosal Technologies Ltd.**, the research joint venture between **Atrix** and **Elan Corp. Plc** (NYSE: ELN), said it has developed an anti-emetic product using the Atrix bioerodible mucoadhesive system prevent nausea and vomiting associated with chemotherapy.

BEMA technology is a pre-formed polymer disc designed for both systemic and local drug delivery across the oral mucosal membranes and can deliver drugs over predetermined time intervals as it erodes, the company said.

"Based on our initial observations in animals, the BEMA system has the potential to get drugs into the bloodstream rapidly without requiring a person suffering from nausea to swallow a tablet," said David Bethune, chairman and CEO of Atrix.

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**Cytyc Corp.** (Nasdaq: CYTC) of Boxborough, MA, said it has entered into an exclusive four-year extension of its agreement with **Dianon Systems Inc.** (Nasdaq: DIAN) of Stratford, CT, to co-promote the Dianon ThinPrep Pap Test as a replacement for the Pap smear.

Dianon said it offers reflex HPV DNA testing with the Digene Hybrid Capture 2 for borderline cytology results.

For mild abnormalities, HPV DNA testing directly from samples collected in ThinPrep Pap Test vials is a highly sensitive method for identifying patients with significant underlying cervical disease, according to a recently published NCI-sponsored study.

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**Epix Medical Inc.** (Nasdaq: EPIX) of Cambridge, MA and **InSightec Ltd.,** of Israel, a developer of devices and software for MRI-guided ultrasound, said they are collaborating with Brigham & Women's Hospital on the Epix MS-325, to treat tumors using MRI guidance.

The preliminary studies may lead to use in the image-guided therapy program at Brigham & Women's Hospital, the company said. Epix and InSightec said they would share information on respective technologies.

"There is significant synergy between the MS-325 ability to prolong tumor enhancement, the InSightec innovative MRI-guided focused ultrasound technique, and Brigham and Women's radiology and interventional expertise," said Michael Webb, CEO of Epix.

"MRI-guided focused ultrasound could revolutionize surgeries to destroy tumors or other unwanted tissues because the method is totally non-invasive, does not require anesthetics, and leaves no surgical scars," said Jakob Vortman, CEO of InSightec. "We are in phase II trials using commercially available MRI contrast agents at five centers for breast cancer and uterine fibroids."

"Compared to existing MRI contrast agents, MS-325 has a much longer plasma half-life, resulting in steady tumor enhancement during procedures, as well as stronger signal enhancement ability," said Ferenc Jolesz, director of the image guided therapy program at Brigham & Women Hospital.

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**NeoPharm Inc.** (Nasdaq: NEOL) of Lake Forest, IL, said it has reached agreement with **NCI** to increase the scope and funding of SS1(dsFv)-PE38 for mesothelin expressing tumors such as head and neck, esophageal, cervical, ovarian and mesothelioma.

Phase I trials of the anti-cancer agent are being conducted for refractory mesothelin modulated cancers, the company said.

"We value our relationship with NCI and look forward to continuing our work with them," said James Hussey, president and CEO of NeoPharm.

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**Peregrine Pharmaceuticals Inc.** (Nasdaq: PPHM) Tustin, CA, said it has extended its radiolabeling research and development agreement with **Paul Scherrer Institut** of Villigen, Switzerland, to include pre-clinical testing of tumor necrosis therapy based positron emission tomography imaging agents

Peregrine has been collaborating with the the Institut to scale-up the radiolabeling processes for its Cotara and Oncolym monoclonal antibody based anti-cancer drugs products, the company said.

"We believe a process is in place to produce commercial quantities of our radiolabeled therapeutic antibodies," said Steven King, vice president of

technology and product development at Peregrine. "PSI will now focus on standardizing and automating the process to ensure reproducibility and quality across manufactured lots. PSI will be able to make research and development progress toward evaluating a TNT based PET imaging agent this year."

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**Pharmaceuticals Inc.** (Nasdaq: MLNM) of Cambridge, MA, and **ImmunoGen Inc.** (Nasdaq: IMGN) said they have entered into a five-year agreement for the ImmunoGen Tumor-Activated Prodrug technology with the Millennium proprietary antibodies.

Each TAP product is comprised of a molecule effector drug that is 100 to 1000 fold more potent than existing chemotherpeutics conjugated to a tumor-targeting monoclonal antibody, the company said. The TAPs are designed to act as prodrugs and remain nontoxic while circulating in the body, only activated once inside the target cell. In preclinical studies, TAPs have shown therapeutic efficacy and complete cures at doses with no detectable toxicity.

The terms agreement call for an undisclosed up-front technology access fee, milestone payments per antigen target, and royalties on net sales of any resulting products, the companies said. Millennium said it would be responsible for product development, manufacturing and marketing of any products developed. ImmunoGen said it may produce preclinical and clinical materialfor manufacturing payments.

The agreement can be renewed for one subsequent three-year period for an additional technology access fee, the companies said.

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**Pharmagene plc** (LSE: PGN) of Royston, U.K. said it has signed a drug discovery agreement with **Bayer Corp**. of Leverkeusen, Germany, in oncology.

Under the terms of the agreement, Pharmagene would identify gene expression patterns across a matrix of diseased and non-diseased human tissue samples, constructed to depict nine cancers for characterising novel therapeutic proteins and antibody targets, the company said. The agreement would cover a defined number of targets but will be expandable.

"Our relationship with Pharmagene is an important part of Bayer's efforts to make sense of the vast quantities of genomic information now available," said Wolf-Dieter Busse, senior vice president for biotechnology at Bayer.

Financial terms were not disclosed.

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**Quest Diagnostics Inc.** (NYSE: DGX) of Teterboro, NJ, and **ProDuct Health Inc**., a privately held company based in Menlo Park, CA, said they are collaborating on a ductal lavage, a cytopathology procedure for early breast evaluation.

Quest Diagnostics said it is the first commercial reference laboratory to accept ductal lavage specimens for analysis. Medicare and most private plans cover the laboratory diagnosis, the company said.

The ProDuct ductal lavage procedure functions like a Pap smear for the breast, allowing the early detection of pre-malignant and malignant cells from their source of origin, the company said.

Nine of the Quest Diagnostics regional laboratories have trained staff to handle ductal lavage specimens using the non-gynecological ThinPrep filtration process as the standard process for preparing the specimens for microscopic slide review.

Specimens are collected using the Product Health InDuct Breast MicroCatheter and InDuct Breast Aspirator, the company said. The system of products enables the collection of cells from the lining of the breast milk ducts for cytological analysis and allows the determination of normal, pre-malignant and malignant cells.

FDA has cleared the devices used in the procedure for medical use, the company said. It will assess high-risk breast cancer patients and is not recommended as a general screening approach.

"The ability to look for the very beginnings of abnormal change in the breast can offer important information for physicians to consider in the management of women at high-risk for breast cancer," said Dwight DeRisi of Long Island Breast Care in Great Neck, N.Y.

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**Xenogen Corp.** of Alameda, CA said it has entered into a six-month evaluation licensing agreement with **Onyx Pharmaceuticals** Inc. (Nasdaq: ONXX) for the Xenogen proprietary real-time, in vivo imaging technology.

Onyx said it would use the technology to image bioluminescent cancer cells in vivo for their virus research programs, image and study the biological activity of genetically engineered viruses that have been engineered to selectively replicate in and lyse cancer cells. The Xenogen technology enables the detection of fluorescent or bioluminescent cells and allows for monitoring NCE efficacy in real time, and also provides methods to localize the activation of selected genes in vivo via LPTA transgenic animals.

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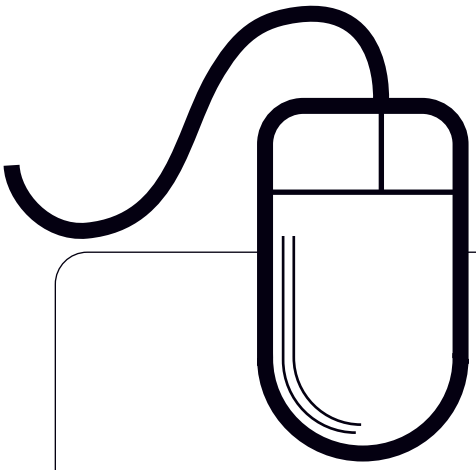

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