THE CANCER LETTER

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Biomedical Research Advocates Temper Budget Requests In View Of War, Deficit

By Kirsten Boyd Goldberg

Biomedical research advocacy groups have tempered their appropriations requests in light of the war in Iraq and the growing budget deficit.

The atmosphere couldn't be more grim at the start of the "appropriations season," the January-to-June Washington ritual which brings Nobel laureates, clinicians, and patients to knock on doors and testify on Capitol Hill.

With the White House seeking $80 billion in additional funding for the war and projecting a $427 billion budget deficit, the salesmanship of

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In Brief:

Varmus Wins ASCO's Science Of Oncology Award; Sawyers To Give Karnofsky Lecture

ASCO announced the recipients of its 2005 Special Awards, given annually to leaders in oncology who have made contributions to cancer care. The awards and lectures will be given at the ASCO annual meeting in May.

The first Science of Oncology Award and Lecture recognizes **Harold Varmus**, president and CEO of Sloan-Kettering Cancer Center. Varmus' research earned him the 1989 Nobel Prize in Medicine or Physiology, with **J. Michael Bishop**, for their discovery that normal human and animal cells contain genes capable of becoming cancer genes.

Charles Sawyers, of Howard Hughes Medical Institute, University of California, Los Angeles, is the recipient of the 2005 David A. Karnofsky Memorial Award and Lecture. The award honors Sawyers for his research on signal transduction in leukemia and prostate cancer.

Barbara Weber, of the University of Pennsylvania Cancer Center, is the recipient of the 2005 American Cancer Society Award and Lecture. The Pediatric Oncology Lectureship Award will be presented to Richard O'Reilly, Sloan-Kettering Cancer Center.

Also receiving awards for contributions to the field are **John Minna**, of the University of Texas Southwestern Medical Center, Distinguished Service Award for Scientific Achievement; **Sharon Murphy**, of the University of Texas Health Science Center at San Antonio, Distinguished Service Award for Scientific Leadership; and **Ron Beller**, chief operating officer, ASCO, Special Recognition Award. Other awards include the Public Service Award, which will be presented to **Joseph Bailes**, for his advocacy on behalf of

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FASEB: NIH Needs 6% Raise To Avoid Program Cuts

(Continued from page 1)

biomedical advocates will be severely tested. The President's budget proposal is expected to be released Feb. 7.

The Federation of American Societies for Experimental Biology, in a recent report advocating an unusually modest 6 percent increase in funding for NIH, laid out its argument:

"FASEB understands that the FY 2006 budget for discretionary spending is projected to be constrained in light of the large deficit, the expenditures for defense and homeland security, and the growth in entitlement obligations. However, FASEB strongly believes that the scientific opportunities for progress in medical research have never been greater.

"The Department of Commerce has projected that the cost of biomedical research will rise by 3.5 percent in FY 2006," the FASEB report said. "Our analysis of current NIH commitments and urgent needs indicated that NIH needs at least a 6 percent increase to avoid curtailment of vital programs."

In requesting $30.07 billion for NIH, the FASEB report noted that "the momentum generated from doubling the NIH budget has energized biomedical science at every level."

"We see new, young investigators making some of the most important discoveries," the FASEB report continued. "Training initiatives have encouraged talented students to choose a career in academic medicine. These highly talented and motivated individuals spend 10 years or more after college in graduate school and postdoctoral appointments.

"In 2003, only 16.6% of new investigators obtained funding within their first three years of applying for these critical grants, thereby making it difficult for these young scientists to establish their new innovative research programs.

"It is impossible to predict which cures and therapies might be lost if funds for medical research are curtailed, but it is certain that inconsistent NIH funding sends a chilling message to young scientists in training and those just entering the research field. Scientific competition will always be intense, but exceptionally talented, young scientists must be assured that sufficient research funding will be available, or they will be forced to pursue alternative careers."

The report, "Federal Funding for Biomedical and Related Life Sciences Research, FY 2006," is available at www.faseb.org.

FASEB is comprised of 22 societies with more than 65,000 members.

Campaign To Raise Limit on Health Programs

Taking a similar approach, the Coalition for Health Funding, a group that represents several academic organizations, is circulating a petition urging the White House and Congress to increase discretionary funding for public health programs by raising the limit on Function 550, the budget allocation that funds all non-entitlement health programs at HHS, including NIH, FDA, CDC, AHRQ, and others.

The coalition wants the Function 550 limit raised by $3.5 billion, or 7 percent, over the current year.

"Many programs need significantly greater growth, but we are trying to restrain our requests at this time, given the realities of budget constraints," said Marcia Mabee, executive director of the coalition.

The $3.5 billion figure "reflects the reality of severe budget constraints and major funding challenges in the coming fiscal year," Mabee said.

"Some coalitions will advocate for a 6 percent increase [for NIH], others for 7 percent, or 8 percent [for other programs], but there is room for everyone if we can boost Function 550," she said.

More than 300 biomedical advocacy organizations, including the American Cancer Society, have signed the petition, which was scheduled to be posted next week at www.aamc.org/advocacy/healthfunding/start.htm.

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HHS News:

EPA Head Michael Leavitt Sworn In As HHS Secretary

Michael Leavitt was sworn in as HHS Secretary Jan. 26. Leavitt is the former head of the U.S. Environmental Protection Agency and a former three-term governor of Utah.

In his remarks before the Senate Finance Committee Jan. 19, during the confirmation hearings, Leavitt described his priorities at HHS.

—**FDA, NIH, and CDC: "**HHS is the trustee for a number of our nation's most treasured brands. A brand is a promise. Over decades, the dedicated scientists and researchers of HHS have earned the public's trust, especially in three brands: FDA, NIH, and CDC.

"To millions of people, these brands are seals of quality, safety, and best in the world research. If they lost their reputations, they would take years to recover. HHS always needs to keep in mind the ethical implications of its decisions, to ensure that Americans can be proud, not only of the department's scientific expertise, but also of the moral judgment of its leaders.

"At FDA, our goal must be to inform consumers about risks and benefits. Our foundation must be sound science. Our motto must be independence.

"At NIH, we must march forward with life-saving research, and always hold the scientists, universities, and laboratories accountable for results.

"At CDC, our guiding focus must be disease prevention and control, sharing generously the best health and safety information in the world."

—**Medicaid: "De**livering health care to the needy is important, but Medicaid is flawed and inefficient. We can do better. We can expand access to medical insurance to more people by creating flexibility for our state partners and transforming the way we deliver it.

—**Medicare Prescription Drug Benefit: "**I have no illusions about the size of the task. It is immense. But I recognize that the President and the Congress made a solemn commitment to America's seniors."

—**Medical Liability Reform: "**Most doctors make a sincere effort to do a good job, but medical errors do occur. People who are harmed by medical errors absolutely deserve prompt and fair compensation. Unfortunately, the capricious liability system that prevails in many states helps no one."

—**Health Care Goals:** "Most broadly, Americans deserve the health care of the twenty-first century. We've earned it. That includes modern medical technology. Modern information technology. And modern, consumer-focused delivery systems.

"I see a world that is rapidly moving toward personalized medicine. People will own their own health savings, health insurance, and health records.

"I see a world in which a doctor can write a prescription on a handheld device and transmit it to the patient's pharmacist, who can start filling it before the patient leaves the doctor's parking lot-and with less chance of error or delay.

"I see a world where doctors heal our loved ones when they are sick, but focus more of their energies on keeping them well in the first place. I see a world where good health care makes America more productive, not less competitive. And I see a world where premier health research serves the betterment of mankind."

Medical Innovation Report

Leavitt succeeds Tommy Thompson, who prior to Leavitt's confirmation, released a report recommending steps the department can take to advance medical innovations and move products more quickly from the lab to the bedside.

The report, "Moving Medical Innovations Forward: New Initiatives from HHS," was the product of an HHS task force formed by Thompson last May to weigh new ideas and promote new solutions to encourage innovation in health care and speed the development of new medical technologies.

The task force examined procedures across the department, including CDC, CMS, FDA, and NIH.

The report made several specific recommendations:

—HHS should enter into new or expanded Memoranda of Understanding to imrpove cooperation with other federal agencies that play an important role in medical technology development.

—HHS should create a forum to serve as a sounding board for investigators and manufacturers to communicate with HHS agencies.

—HHS should support the development of standard formats for electronic clinical trial data.

—Improved cooperation between CMS and FDA.

—New interagency scientific education and cross-training efforts should be supported to identify knowledge gaps among those serving in the technology transfer functions in HHS.

FDA Acting Commissioner Lester Crawford served as chairman of the task force.

The report is available at www.hhs.gov/reference/medicalinnovations.shtml.

ImClone:

SEC To Settle With Waksals For More Than $5 Million

By Paul Goldberg

Former ImClone Systems Inc. executive Samuel Waksal and his father Jack Waksal agreed to pay over $5 million to settle an insider trading case with the Securities and Exchange Commission.

In a related development, ImClone agreed to pay $75 million in a consolidated class action suit claiming violations of securities laws involving the company's claims about the drug Erbitux.

Samuel Waksal, a former CEO, is serving a 87-month prison sentence for securities fraud. His friend and ImClone investor Martha Stewart is also serving a prison sentence for obstructing an investigation of her stock sales.

In their settlement with SEC, the Waksals agreed to a disgorgement of $2.02 million in "illegal loss avoidance," the commission said. Further, Sam Waksal would be liable for a civil penalty of about $3.02 million, SEC said, announcing the settlement Jan. 19.

In March 2003, in a partial resolution of the case, Samuel Waksal agreed to disgorge $800,000 and agreed to be permanently barred from acting as an officer of a public company.

SEC originally filed insider trading charges against Samuel Waksal in June 2002, and added Jack Waksal as a defendant on October 2003.

The commission charged that in late December 2001, Samuel Waksal learned that FDA would refuse to file the Erbitux application, and before the news became public attempted to unload his own ImClone stock and purchased ImClone put option contracts, betting on a drop in his company's stock price.

Meanwhile, Samuel Waksal's daughter Aliza sold all her ImClone stock, and Jack Waksal was selling ImClone stock from his own account and from the account of his daughter Patti Waksal.

According to SEC, the payment would be made without admission or denial of the allegations. In a statement to the press, Samuel Waksal's attorney Lewis Liman said his client "deeply regrets this period in his life" and "he is glad to have resolved this matter amicably and to have it behind him and his family."

Announcing the settlement of the consolidated shareholders' suit Jan. 24--Irvine v. ImClone Systems Inc.—the company said it would continue to pursue its claims against Samuel Waksal, who, the company said earlier, failed to pay taxes owed on sale of ImClone stock.

Under the settlement agreement, all claims against the company and members of its board of directors would be dismissed. In addition to making a payment to shareholders, the company agreed to amend the charter of its Research Oversight Committee to provide that the committee would meet regularly with the officer responsible for interaction with FDA.

ImClone said its would make a $55.4 million charge against its fourth quarter 2004 earnings to cover the settlement. "The principal terms of the Irvine settlement provide for an aggregate cash payment to class members of $75 million, a portion of which will be paid by the company's insurance carriers," ImClone said.

The company said it expects that insurance carriers would contribute $8.75 million to the settlement.

NCI Programs:

10 Centers Win Recompetition, Program Up $11M From FY03

By Kirsten Boyd Goldberg

NCI allocated $233.6 million in FY 2004 to fund 61 Cancer Center Support Grants.

The allocation represents a 4.7 percent increase ($11 million) over the previous year.

Centers that competed successfully last year to renew their CCSGs, also known as "core" grants, were:

—Salk Institute for Biological Sciences

—Dartmouth College

—Mayo Clinic Rochester

—Burnham Institute

—Huntsman Cancer Institute at University of Utah

—Washington University

—Indiana University-Purdue University at Indianapolis

—University of Pittsburgh

—Vanderbilt University

—University of Nebraska Medical Center

The recompeting centers were funded on a sliding scale based on priority score, the same method NCI used last year (**The Cancer Letter**, Jan. 16, 2004).

There were no changes in the number of centers funded between FY 2003 and 2004. No center lost its CCSG and no new centers were added.

The following table lists the FY04 cancer center awards by state as generated by the NCI Financial Management Branch.

Cancer Centers by State (P30 Core Grants), Fiscal Year 2004

(Dollars in Thousands)

State	Grantee Institution	Type	Amount
Alabama	University of Alabama at Birmingham	Comprehensive	$5,525
California	Beckman Research Institute	Comprehensive	2,480
	Burnham Institute	Lab/Basic	3,400
	Salk Institute for Biological Sciences	Lab/Basic	2,900
	University of California Davis	Clinical	1,334
	University of California Irvine	Comprehensive	2,599
	University of California Los Angeles	Comprehensive	4,584
Colorado	University of Colorado Health Sciences Center	Comprehensive	3,563
Connecticut	Yale University	Comprehensive	1,039
District of Columbia	Georgetown University	Comprehensive	2,832
Florida	University of South Florida/ H. Lee Moffitt Cancer Center	Comprehensive	2,410
Hawaii	University of Hawaii at Manoa	Clinical	2,125
Illinois	Northwestern University	Comprehensive	4,873
	University of Chicago	Clinical	3,788
Indiana	Indiana University - Purdue University at Indianapolis	Clinical	1,200
	Purdue University West Lafayette	Lab/Basic	1,262
Iowa	University of Iowa	Comprehensive	1,373
Maine	Jackson Laboratory	Lab/Basic	2,775
Maryland	Johns Hopkins University	Comprehensive	5,975
Massachusetts	Dana-Farber Cancer Institute	Comprehensive	10,514
	Massachusetts Institute of Technology	Lab/Basic	2,551
Michigan	University of Michigan at Ann Arbor	Comprehensive	5,184
	Wayne State University	Comprehensive	500
Minnesota	Mayo Clinic Rochester	Comprehensive	5,000
	University of Minnesota Twin Cities	Comprehensive	3,350
Missouri	Washington University	Clinical	4,062
Nebraska	University of Nebraska Medical Center	Clinical	1,522
New Hampshire	Dartmouth College	Comprehensive	2,944
New Jersey	Robert Wood Johnson Medical School	Comprehensive	2,550
New York	American Health Foundation/ Inst for Cancer Prevention	Lab/Basic	2,713
	Cold Spring Harbor Laboratory	Lab/Basic	3,855
	Columbia University Health Sciences	Comprehensive	1,842
	Kaplan Cancer Center/NYU	Clinical	2,575
	Roswell Park Cancer Institute Corp	Comprehensive	3,781
	Sloan-Kettering Institute for Cancer Research	Comprehensive	9,943
	Yeshiva University	Clinical	3,928
North Carolina	Duke University	Comprehensive	5,838
	University of North Carolina Chapel Hill	Comprehensive	5,544
	Wake Forest University	Comprehensive	1,322
Ohio	Case Western Reserve University	Comprehensive	4,318
	Ohio State University	Comprehensive	2,757
Oregon	Oregon Health & Science University	Clinical	1,260
Pennsylvania	Fox Chase Cancer Center	Comprehensive	7,952
	Thomas Jefferson University	Clinical	4,441
	University of Pennsylvania	Comprehensive	5,543
	University of Pittsburgh at Pittsburgh	Comprehensive	5,000
	Wistar Institute	Lab/Basic	2,664
Tennessee	St. Jude Children's Research Hospital	Clinical	4,970
	Vanderbilt University	Comprehensive	5,100
Texas	San Antonio Cancer Institute	Clinical	2,834
	University of Texas M.D. Anderson Cancer Center	Comprehensive	9,497
Utah	Huntsman Cancer Institute/University of Utah	Clinical	800
Vermont	University of Vermont & St. Agric College	Comprehensive	1,348
Virginia	University of Virginia Charlottesville	Clinical	1,065
	Virginia Commonwealth University/Massey Cancer Center	Clinical	1,865
Washington	Fred Hutchinson Cancer Research Center	Comprehensive	9,927
Wisconsin	University of Wisconsin Madison	Comprehensive	5,521
	Total P30s	61	233,648

Capitol Hill:

Feinstein, Hutchison to Renew Breast Cancer Research Stamp

Legislation to reauthorize the special fundraising Breast Cancer Research Stamp was introduced in Congress earlier this week by Sens. Dianne Feinstein (D-Calif.) and Kay Bailey Hutchison (R-Texas).

The stamp is scheduled to expire at the end of this year.

"The Breast Cancer Research Stamp has raised more than $42 million for research into treatments for this terrible disease," Feinstein said. "Breast cancer affects millions of people in this country and the funds raised by this stamp can help more of them to become cancer survivors and not cancer victims. I urge my colleagues to join me in the effort to continue this remarkable stamp."

The stamp was first issued in 1998. The U.S. Postal Service has sold 588.3 million of the stamps.

The stamp costs 45 cents and is deemed valid as a 37-cent stamp. The additional 8 cents charged for each stamp is directed to research programs at NIH, which receives 70 percent of the proceeds, and the Department of Defense breast cancer research programs, which receives the remaining 30 percent of the proceeds.

"Congress should make sure this program can continue advancing this critical work," Hutchison said. "I am proud to again partner with my friend Senator Feinstein in this effort and I am hopeful our colleagues will support this important legislation."

Congress has reauthorized the stamp three times since its inception.

Funding Opportunities:

Program Announcements

PA-05-041: Small Business Innovation Research and Small Business Technology Transfer to Improve The Chemistry and Targeted Delivery of RNAi Molecules

Notice: The PA must be read in conjunction with the Omnibus Solicitation of NIH, Centers for Disease Control and Prevention, and FFDA for Small Business Innovation Research and Small Business Technology Transfer Grant Applications. The solicitation (see http://grants.nih.gov/grants/funding/sbirsttr1/index.pdf or http://grants.nih.gov/grants/funding/sbirsttr1/index.doc).

Application Receipt Date(s): Standard dates apply, see http://grants.nih.gov/grants/funding/submissionschedule.htm.

Participating institutes of NIH invite applications from the small business community to develop approaches and chemical modifications to increase the long term stability, delivery and targeting of siRNAs in cells and tissues for laboratory and therapeutic applications. Therapeutic applications of RNAi are broad and far reaching, ranging from acquired diseases, such as viral infections, to genetic disorders, particularly where there is a dominant gain-in-function mutation. Promising results in gene silencing have already been shown either in vitro or in vivo for viral diseases (such as HIV/AIDS, influenza, human papillomavirus infection, various hepatitis strains, smallpox, and SARS), neurodegenerative diseases (such as Parkinson's disease, amyotrophic lateral sclerosis, spinocerebellar ataxia, and Alzheimer's disease), cancer, inflammatory diseases (such as rheumatoid arthritis), and autoimmune diseases (such as type 1 diabetes mellitus). The PA uses the SBIR and STTR mechanisms. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-05-041.html.

Inquiries: For NCI--Suresh Arya, NCI, Division of Cancer Treatment and Diagnosis, phone 301-496-8783; fax 301-402-5200; e-mail aryas@exchange.nih.gov.

PA-05-040: Molecular Approaches to Diet and Pancreatic Cancer Prevention

Application Receipt Dates: Standard dates apply, http://grants.nih.gov/grants/funding/submissionschedule.htm.

The initiative invites preclinical and clinical R01 applications to determine how dietary energy intake and bioactive food components, including alcohol, influence pancreatic cancer development and prevention. The PA encourages collaboration between nutritional scientists and cancer biologists, oncologists and gastroenterologists to examine mechanisms in the pancreatic cancer process (e.g., carcinogen metabolism, cell division, differentiation, apoptosis) to establish mechanistic links between quantity and form of energy consumed and/or bioactive food component intakes with pancreatic tumor incidence and behavior. The linkage between diet and pancreatic cancer comes from its long-recognized interrelationships with diabetes and obesity, and thus with caloric intake and expenditure. The PA seeks to expand research that will clarify the importance of diet-related energetics and bioactive food components in pancreatic cancer prevention. Specifically, preclinical and clinical studies are sought that utilize innovative molecular biological approaches to determine the importance of energy intake and/or bioactive food constituents as site-specific modifiers of the pancreatic cancer process.

Some of the mechanistic pathways leading to pancreatic cancer involve: insulin signaling pathways, the impact of glycated proteins, free radical damage, and aberrant methylation processes. The discovery, identification, and characterization of the roles of dietary components in regulating these and other biological processes in the development of pancreatic cancer deserve further study, and serve as the basis of this PA. Additionally, understanding the underlying molecular, biochemical, and cellular mechanisms by which alcohol ingestion leads to the development of pancreatitis and subsequent pancreatic cancer risk also is a

relevant topic. Illustrative examples for the development of R01 applications include, but are not limited to, the following examples: nutritional genomic, epigenomic, proteomic, and metabolomic approaches to examining energy metabolism and/or bioactive food component activity in relevant pancreatic cancer models; genetic polymorphisms in energy metabolism that affect risk of pancreas cancer and interact with diet; mechanistic studies about the impact of oxidative stress, dietary antioxidants and pancreatic cancer (e.g., apoptosis, IGF-1 signaling); impact of insulin resistance and associated factors (including BMI, obesity, energetics) on risk of developing pancreatic cancer; Understanding synergistic relationships between bioactive food components in relevant pancreatic cancer signaling pathways; development of relevant animal models for pancreas cancer and application of such models to dietary studies of pancreatic cancer prevention; examining the metabolic syndrome as a trigger in early onset of pancreatic cancer; understanding the molecular mechanisms by which dietary fat, oxidative stress, acetaldehyde, cytokines, and other factors contribute to the pathogenesis of chronic alcoholic pancreatitis; and examining the role of chronic alcoholic pancreatitis in the development of pancreatic cancer.

The PA will use the NIH investigator-initiated research project grants R01 award mechanism. Investigators interested in submitting Small Grants Program grant applications R03 on this topic are directed to use the Small Grant Program opportunity listed at http://grants.nih.gov/grants/guide/pa-files/PAR-04-147.html. This PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-05-040.html.

Inquiries: For NCI--Scientific/Research Contacts: Sharon Ross, Division of Cancer Prevention, phone: 301)-594-7547; fax 301-480-3925; e-mail rosssha@mail.nih.gov.

Request for Information

NOT-CA-05-010: Comprehensive Identification of Tumor Mutations: Request for Information

Closing Date: Feb. 25

NIH is seeking input from the community on the large-scale identification of somatic mutations in cancer through the comparison of sequences of multiple tumor samples to reference sequence from normal tissue from the same individuals. The hypothesis is that the identification of somatic mutations will accelerate the development and application of diagnostic and therapeutic approaches for the prevention, diagnosis, and treatment of cancer.

The RFI is for analysis and planning purposes only and should not be construed as a solicitation or as an obligation on the part of the government. The notice is available at http://grants.nih.gov/grants/guide/notice-files/NOT-CA-05-010.html.

Inquiries and Comments: Daniela Gerhard, acting director , Office of Cancer Genomics, NCI, phone: 301-451-8027, Or, Cyndy Izadi, administrative program assistant, e-mail izadic@mail.nih.gov; fax 301-480-4368.

In Brief:

Monica Morrow Named Editor Of ASCO Daily News

(Continued from page 1)

ASCO for better cancer care policies and legislation. The Partners in Progress Award will be given to **Carolyn Aldigé**, president and founder of the Cancer Research and Prevention Foundation.

The award recipients were chosen by the ASCO Special Awards Selection Committee, chaired by **Margaret Tempero**, immediate past president of ASCO.

* * *

Monica Morrow, chairman of surgical oncology at Fox Chase Cancer Center and the G. Willing Pepper Chair in Cancer Research, was named editor of the ASCO Daily News. She replaces **Bruce Cheson**, who held the position since the establishment of the annual meeting newspaper in 1998.

To make the newspaper a more valuable resource for meeting attendees, Morrow said she plans to bring a variety of enhancements to the newspaper over her five-year term, many of which are based on feedback from a member survey conducted last year.

Morrow served on the ASCO Board of Directors (1998-2001), and has been a member of several committees, including the Program Committee, the Patient Advocacy Committee, the By-Laws Committee, the CME Committee, the Surgical Oncology Task Force, and the Cancer Communications Committee. She is also the immediate past chairman of the Publications Committee.

Her editorial experience includes her role as surgical editor of the multiauthored textbook, "Diseases of the Breast," and the sixth edition of the AJCC Cancer Staging Manual. She is an associate editor of the "Yearbook of Oncology," the North American editor of the journal The Breast, and serves on the editorial boards the Journal of the American College of Surgeons, Cancer, and the Journal of Clinical Oncology.

Before joining Fox Chase Cancer Center last year, Morrow was professor of surgery at the Northwestern University Feinberg School of Medicine and director of Clinical Breast Programs, including the Lynn Sage Comprehensive Breast Center, Northwestern Memorial Hospital.

The appointment of Morrow is the result of a search conducted by a subcommittee of the Publications Committee, led by **Karen Kelly**, chairman of the committee.

* * *

NEVADA CANCER INSTITUTE received a $25 million challenge grant from The Greenspun Family Foundation, said **Nicholas Vogelzang,** director of NVCI. The grant is the largest ever for NVCI and comes two years after the founding of the institute. In addition to the grant, The foundation gave the institute a $5 million gift last July. The $25 million challenge grant also comes a year after Vogelzang was appointed director of the institute and six months after **David Ward** was appointed deputy director. "With this challenge grant, we hope to inspire others to invest in Nevada by providing financial support for this historic and worthwhile cause," said **Brian Greenspun**, president and editor of the Las Vegas Sun, and director of foundation. "Large scale gifts such as this are very important not only to our research efforts but also moral-boosting," said Vogelzang. . . . **ELIZABETH NABEL** was named director of the National Heart, Lung, and Blood Institute. She is known for her research in the development of genetic and cellular therapies for cardiovascular disease. Nabel, who is scientific director of clinical research in the NHLBI intramural program, will begin her appointment on Feb. 1. . . . **HELFORD CLINICAL RESEARCH Hospital** at City of Hope is scheduled to open Feb. 13. The 347,000-square-foot, seven-floor building includes six surgical supersuites, each 600 square feet in size; antimicrobial AgION steel to minimize risk of opportunistic infection; an integrated model for clinical practice; and a streamlined medication dispensing system. Also, City of Hope Cancer Center announced the appointments of staff members in the Department of General Oncologic Surgery. **Alessio Pigazzi**, **Jeannie Shen** and **Vijay Trisal** were named clinical assistant professors, Department of Oncologic Surgery. All three recently completed fellowship training. . . . **INTERNATIONAL SOCIETY for Biological Therapy of Cancer** announced the winners of the 2004 Presidential Award. **Luca Gattinoni**, of the NCI Surgery Branch, and **Jiali Li**, of Stanford University, were co-award winners in the abstract competition, said **Michael Atkins**, president of iSBTc. Gattinoni worked in the NCI laboratory of **Nicholas Restifo**. Li worked in the laboratory of **Ronald Levy** at Stanford. The young investigators received plaques and accompanying checks from the iSBTc for $1,000 at the iSBTc presidential reception in November. . . **JAMES GRAHAM BROWN Cancer Center** at University of Louisville received a commitment of a five-year, $15 million gift from the James Graham Brown Foundation. "This is the largest gift ever to the University of Louisville, tied only with the Brown Foundation's $15 million gift to the cancer center in 2001," said **James Ramsey**, president of the University of Louisville. Also, **Patty Melvin** was named vice president for cancer operations at the center. She was vice president at Western Pennsylvania Hospital, in Pittsburgh, with primary responsibility for the department of Medicine, including Oncology/BMT services. **Douglas Dean** was named the Rounsavall Chair of Ocular Cancer Biology by the center. Dean, of Washington University, has appointments in the cancer center and the Department of Ophthalmology. . . . **MARY KERR** was appointed deputy director of the National Institute of Nursing Research, said **Patricia Grady**, director of NINR. Kerr was UPMC Health System chairman in nursing science, School of Nursing, University of Pittsburgh. Her primary appointment was professor, Department of Acute & Tertiary Care Nursing, School of Nursing, with a secondary appointment of professor, Department, of Neurological Surgery in the School of Medicine. She also was associate director, clinical core, Brain Trauma Research Center at UPMC. . . . **BRUCE GORDON,** associate professor of pediatrics and co-chairman of the Institutional Review Board at the University of Nebraska Medical Center, has been appointed to the Secretary's Advisory Committee on Human Research Protections Subpart A Subcommittee at the HHS Office of Human Research Protections. SACHRP advises the secretary on research involving human subjects. As part of the subcommittee, Gordon and 12 others will recommend how regulations should be interpreted or whether they need to be modified. Gordon, a pediatric oncologist, was named chairman of the NCI Pediatric Central Institutional Review Board in 2004. He became a member of the UNMC IRB in 1992 and has been its chairman for seven years. . . . **ROBERT HANSON**, vice president of resource development for the United Way of Central Ohio, has joined the staff of The Ohio State University Arthur G. James Cancer Hospital and Richard J. Solove Research Institute as associate director of development. Hanson will focus his efforts on cultivating business, community and philanthropic support for Project Cancer, a campaign to expand the Ohio State cancer program. . . . **INTERNATIONAL GENOMICS CONSORTIUM** Expression Project for Oncology released clinically annotated gene expression profiles for 60 tumor specimens, completing the initial phase of the nation's first public database dedicated to standardized gene expression data. The clinically annotated dataset is available at www.ncbi.nlm.nih.gov/geo/.

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Business & Regulatory Report

Product Approvals & Applications:

Kepivanc Approved For Oral Mucositis; FDA Approves Clofarabine For ALL

FDA approved Kepivanc (palifermin), for severe oral mucositis associated with high-dose chemotherapy, with or without radiation, followed by a bone marrow transplant. The agent is sponsored by **Amgen Inc.** (Nasdaq: AMGN) of Thousand Oaks, Calif.

Kepivance, a recombinant human keratinocyte growth factor that works at the cellular level, reduces severe oral mucositis by protecting the epithelial cells that line the mouth and throat from the damage caused by chemotherapy and radiation and by stimulating the growth and development

(Continued to page 2)

Clinical Trials:

ImClone Testing Monoclonal Antibodies; Montreal Firm Begins Early Trial For CLL

Dyax Corp. (Nasdaq: DYAX) of Cambridge, Mass., said two fully human monoclonal antibodies that were derived from its proprietary phage display libraries have entered into phase I development at **ImClone Systems**.

ImClone said the antibodies, IMC-11F8 and IMC-1121B, both of which target growth factor receptors, are being evaluated as cancer therapeutics. Each antibody was isolated using an antibody-fragment phage display library licensed to the company by Dyax, and then further optimized by ImClone Systems.

IMC-11F8, a fully human monoclonal antibody, is designed to bind to the epidermal growth factor receptor, thereby inhibiting certain ligands known as growth factors from binding to and activating the receptor, the company said. The action blocks a signal pathway to tumor growth and repair, and, has also been shown to induce cell death, or apoptosis, in human tumors in animal models, ImClone Systems said. IMC-11F8 has begun phase I development in Europe.

IMC-1121B, also a fully human monoclonal antibody, targets vascular endothelial growth factor receptor-2, which is present on endothelial cells and forms blood vessels in solid tumors, the company said. Inhibition of the function of the receptor with IMC-1121B blocks angiogenesis, thereby limiting nutrient supply to the tumor and causing tumor cell death in preclinical models, said ImClone Systems. IMC-1121B has begun phase I development in the U.S.

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Gemin X Biotechnologies Inc. of Montreal said it received orphan

(Continued to page 4)

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FDA Approves Kepivance, Clofarabine, And Prialt

(Continued from page 1)

of new epithelial cells to build up the mucosal barrier, the company said. The safety and efficacy of Kepivance have not been established in patients with non-hematologic malignancies.

"Until now, severe painful oral mucositis has been considered an unmet medical need for which no effective therapies existed to reduce either its incidence or duration," said Patrick Stiff, director of the Cardinal Bernardin Cancer Center, Loyola University Health System and professor of hematology/oncology, Loyola University Chicago Stritch School of Medicine, and a lead investigator in the trial. "The most we could do for our patients was to give them ice chips and narcotics to try and manage their pain."

In a phase III double-blind study that compared Kepivance with placebo in the development of oral mucositis with hematologic malignancies, participants were randomized to receive the drug 60 micro-g/kg/day (n=106) or placebo (n=106) intravenously for three consecutive days immediately before conditioning therapy (fractionated total body radiation plus high-dose chemotherapy). Then all received bone marrow transplantation, followed by an additional three days of either the agent or placebo, the company said.

The incidence of grade 4 mucositis was three times lower with Kepivance (20 percent versus 62 percent with placebo), and the incidence of grade 3-4 mucositis was reduced by approximately one-third (63 percent versus 98 percent with placebo), the company said. The drug reduced the duration of oral mucositis (grades 2-4) by almost half, or approximately one week (8 days versus 14 days with placebo).

Treatment yielded less mouth and throat soreness, as well as improvements in the to eat, drink, swallow and talk, the company said. In addition, treatment with Kepivance required fewer days of morphine for pain compared to treatment with placebo (7 days versus 11 days, respectively).

The agent was shown to be safe and well-tolerated, the company said. Adverse events including rash, pruritus, erythema, paresthesia, mouth/tongue disorders and taste alteration were mild-to-moderate and transient.

* * *

FDA granted marketing approval for Clofarabine for children with refractory or relapsed Acute Lymphoblastic Leukemia. The agent's sponsor is **Bioenvision Inc.** (Nasdaq: BIVN) of New York.

Clofarabine is indicated for pediatric patients 1 to 21 years of age with relapsed or refractory ALL after at least two prior regimens, the company said.

The FDA approval follows the recommendation by the Oncology Drug Advisory Committee last December (**The Cancer Letter**, Dec. 10, 2004).

Clofarabine was previously granted orphan drug designation for adult and pediatric ALL and AML, in the US and in Europe. In the U.S., orphan drug status extends seven years of market exclusivity for the orphan drug indication following the FDA marketing approval, the company said. FDA also recently granted an additional six months market exclusivity to Clofarabine under the Best Pharmaceuticals for Children Act. In Europe, this designation provides European marketing exclusivity for 10 years.

Clofarabine is a next generation of the drug class purine nucleoside analogs which all inhibit DNA production for cancer cell growth, the company said.

Bioenvision Inc. said it had sub-licensed **Genzyme** the right to develop and market Clofarabine for cancer in the U.S. and Canada. Bioenvision received milestone payments tied to the development of the compound and is entitled to royalties on North American sales.

Bioenvision originally obtained clofarabine development and commercialization rights under patents held by Southern Research Institute. The company is developing clofarabine in the rest of the world.

* * *

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FDA approved Prialt (ziconotide intrathecal infusion) for severe chronic pain where intrathecal therapy is warranted, and where there is intolerance to other treatment, such as systemic analgesics, adjunctive therapies or IT morphine. Prialt is sponsored by **Elan Corp. plc** of Dublin, Ireland.

Approval was based on three phase III trials of 1,200 patients, which evaluated the efficacy and safety of IT the agent where severe chronic pain was not adequately managed despite a regimen of systemic and/or IT analgesic and other drugs, the company said.

Prialt is a non-opioid analgesics known as an N-type calcium channel blocker. It is the synthetic equivalent of a naturally occurring conopeptide found in a marine snail known as Conus magus. Research suggests the mechanism of action works by targeting and blocking N-type calcium channels on nerves that ordinarily transmit pain signals, the company said.

The most recent randomized double-blind, placebo-controlled study was conducted at 39 sites in the U.S. in response to the FDA approvable letter in 2001, which requested additional data using lower doses and a slower titration company said. 220 adults with opioid-resistant, severe chronic pain were enrolled for up to nine weeks. Most of the patients had neuropathic pain. All patients had programmable IT infusion systems and were randomized to receive IT prialt (n=112) or placebo (n=108). At baseline, the mean visual analog scale of pain intensity score, for both placebo and prialt groups was 80.7 mm. (VASPI score of 0 mm = no pain; 100 mm = worst possible pain). Treatment was initiated at 2.4 mcg/day (0.1 mcg/hour) and was increased by less than or equal to 2.4 mcg/day (less than or equal to 0.1 mcg/hour), no more than two to three times a week for three weeks, the company said.

The primary efficacy measure was mean percent change in the VASPI score at week three, which showed statistically significant improvement in patients receiving Prialt vs. placebo ($p=0.036$), the company said. Improvement in VASPI score was seen as early as week one. The mean dose at week three was 6.9 mcg/day (0.29 mcg/hour). The majority of secondary efficacy endpoints also showed statistically significant improvement with the drug.

The majority of adverse events were mild or moderate, the company said. The four most frequently reported adverse events were dizziness, ataxia, confusion, and abnormal gait, the company said. Study discontinuation amongst the Prialt group due to adverse events was comparable with that for placebo (5.4 percent and 4.6 percent, respectively).

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Advanced Viral Research Corp. (OTC Bulletin Board: ADVR) of Yonkers, N.Y., said it has received an IND license for the systemic use of AVR118 for advanced malignancies.

AVR118 is a biopolymer that has immunomodulator activity, the company said. The peptide-nucleic acid complex stimulates the pro-inflammatory responses to combat viral infections such as HIV and human papillomavirus and to dampen aberrant autoimmune-type inflammatory responses, including rheumatoid arthritis. AVR118 has activity against fatigue, loss of appetite, and weight loss in patients with HIV, the company said.

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MGI Pharma Inc. (Nasdaq: MOGN) of Minneapolis and **SuperGen Inc.** (Nasdaq: SUPG) of Dublin, Calif., said the new drug application of Dacogen (decitabine) for injection was accepted for filing by FDA.

The NDA included clinical data from one phase III trial of Dacogen injection for MDS in addition to two phase II studies, the companies said. The co-primary endpoints of the phase III study were response rate and time to AML transformation or death.

The trial achieved the co-primary endpoint of overall response rate, the company said. The Dacogen arm of the trial had a response rate of 17 percent as determined by intent to treat analysis, compared to a 0 percent response rate those who received supportive care ($p<0.001$).

Responses were durable and lasted a median of nine months, and all patients who responded to Dacogen therapy remained or became transfusion independent. Median time to progression to AML or death was 340 days for treatment with the injection, compared to a median of 219 days for the supportive care arm, which was not statistically significant, the companies said.

Dacogen injection is a DNA methyltransferase inhibitor. DNA methylation is a process in which methyl groups are added to DNA to inactivate genes, the companies said.

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Rejuvenon Corp. of Bridgewater, N.J., said it has received a Fast Track designation from FDA for its investigational compound, RC-1291, a small-molecule ghrelin mimetic, for cachexia and anorexia for cancer.

Ghrelin is a small endogenous protein that acts on the growth hormone secretagogue receptor, a G-Protein Coupled Receptor recognized as a control point in the growth hormone signaling pathway. It is administered

by injection.

RC-1291 is a synthetic, small-molecule ghrelin mimetic that binds to, and stimulates, the GHSR. Unlike ghrelin, RC-1291 is administered once daily by mouth, the company said. The compound has been studied in a series of seven completed or ongoing clinical studies, including a double-blind placebo-controlled study in which, compared to placebo, RC-1291 significantly increased appetite and spontaneous food intake, the company said.

Clinical Trials:

Merck Begins Phase I Trial Of VX-680 For Solid Tumors

(Continued from page 1)

drug designation for and has begun a phase I/II trial of GX15-070 for chronic lymphocytic leukemia.

The treatment induces apoptosis by inhibiting the Bcl-2 family of proteins in CLL, the company said.

The open-label, dose-escalation study would evaluate the safety and tolerability of multiple doses of GX15-070, the company said. The trial would also include extensive pharmacokinetic sampling and pharmacodynamic evaluation. The drug would be administered once every three weeks for CLL where treatment with an alkylating agent and Fludarabine has already taken place.

"GX15-070 is the first small molecule in human trials that targets Bcl-2 proteins, which are involved in many types of cancers," said Thomas Kipps, deputy director of the Comprehensive Cancer Center and head of the CLL Research Consortium at UCSD. "In particular, some members of the Bcl-2 family are thought to play a significant role in the etiology of CLL, making this disease a logical choice as a development indication. I look forward to evaluating the compound's potential in this patient group."

GX15-070 is also being studied in a separate phase I trial various solid tumor cancers, the company said.

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Merck & Co. Inc. of Whitehouse Station, N.J., and **Vertex Pharmaceuticals Inc.** of Cambridge, Mass., said they have begun a phase I study for VX-680, a small molecule inhibitor of Aurora kinases, for solid tumor cancers.

The open-label, dose-escalation study conducted at two cancer treatment centers evaluated the safety and tolerability of the inhibitor when administered in multiple cycles for solid tumors refractory to prior chemotherapy treatment.

Along with clinical development, Vertex and Merck are conducting a joint research program to characterize the activity of VX-680 across cancer types targeting the Aurora kinases, the companies said.

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Pro-Pharmaceuticals Inc. (Amex: PRW) of Newton, Mass., said it has completed the enrollment in a phase I 40-patient trial of Davanat alone and in combination with 5-Fluorouracil in refractory patients with solid tumors.

Jyotsna Fuloria, of the Ochsner Cancer Institute in New Orleans, is principal investigator, the company said.

Davanat is a proprietary polysaccharide that delivers chemotherapy drugs to protein receptors in cancer cells, the company said.

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Threshold Pharmaceuticals Inc. of South San Francisco said it has initiated patient enrollment for a phase I/II trial evaluating the dosing, safety and activity of Glufosfamide in combination with gemcitabine for advanced solid malignancies or as a first line treatment for pancreatic cancer.

The phase I trial of 15 patients would evaluate various doses of Glufosfamide in combination with the standard dose of gemcitabine for any kind of advanced solid malignancy for which gemcitabine is a treatment option, the company said. The maximum tolerable dose combination determined in the 47-patient study would be used in the phase II portion for pancreatic cancer at sites in the U.S. and Latin America.

Earlier this year, Threshold said it had begun a phase III trial to evaluate Glufosfamide where metastatic pancreatic cancer was refractory to first-line treatment. The data from that trial would be evaluated under a Special Protocol Assessment granted by FDA, the company said.

Deals & Collaborations:

ImClone Signs Agreements With Genentech, Centocor

ImClone Systems Inc. (Nasdaq: IMCL) of New York signed license agreements with Genentech (NYSE: DNA) and Centocor Inc. (a Johnson & Johnson Company) for the rights to patents covering various aspects of antibody technology.

The Genentech patents are U.S. Patent 4,816,567, and U.S. Patent 6,331,415, also known as the Cabilly patents, and U.S. Patent 5,770,195, a use patent involving epidermal growth factor receptor, known as

the Hudziak patent.

The Centocor patent is U.S. Patent 5,807,715, known as the Morrison patent.

These licenses relate to Erbitux, an IgG1 monoclonal antibody approved for use in irinotecan resistant or refractory, EGFR-expressing metastatic colorectal cancer, and IMC-11F8, an investigational fully-human EGFR-targeted antibody currently in phase I clinical testing.

For Erbitux use in combination with anti-neoplastic agents, ImClone Systems' gross royalty expense for all licenses, including Genentech, Centocor, Aventis and the University of California, is approximately 12.75 percent of North American sales and is effective from Feb. 24, 2004, the company said.

ImClone said it receives reimbursements for a portion of these royalty expenses, resulting in a net royalty expense to ImClone Systems of 8.25 percent. After the first quarter of 2006, gross royalty expense will decrease to 9.75 percent and net royalty expense will decrease to 7.25 percent, the company said.

For Erbitux monotherapy use, gross and net royalty expenses will be reduced because certain licenses are not applicable, the company said. For sales outside of North America, of Erbitux manufactured in the U.S., such expenses will be passed through to ImClone Systems' partner Merck KGaA as a component of cost of goods for commercial product.

"We are pleased to have concluded these negotiations and to be in a position to give greater clarity to our investors with regard to our Erbitux royalty expenses," ImClone CEO Daniel Lynch said in a statement.

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Abgenix Inc. (Nasdaq: ABGX) of Fremont, Calif., said it would receive a milestone payment from **Amgen Inc.** triggered by the Amgen advancement of an undisclosed antibody, created using the Abgenix proprietary XenoMouse technology, into clinical trials.

This is the eleventh antibody generated with the Abgenix technology to move into the clinic phase, the company said.

In 1999 Abgenix entered into an agreement with Amgen granting Amgen a license to its antibody generation technology, the company said. Amgen is responsible for product development and commercialization of any products developed through the collaboration. Abgenix may receive milestone payments and royalties of any future product sales. Abgenix and Amgen have a separate co-development agreement for panitumumab, an EGFr inhibiting fully human monoclonal antibody that is currently in pivotal trials as a third line monotherapy for colorectal cancer, the company said.

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Allos Therapeutics Inc. (Nasdaq: ALTH) of Westminster, Colo., said it has acquired an exclusive worldwide license from the **University of Colorado Health Sciences Center,** the **University of Salford** and **Cancer Research Technology** to develop and commercialize RH1, a chemotherapeutic agent.

The compound is in a phase I trial sponsored by Cancer Research UK, the company said.

RH1, which was a nominated compound for advancement in the NCI Developmental Therapeutics Program, is a targeted cytotoxic prodrug that is bioactivated by the enzyme DT-diaphorase, the company said. The enzyme is over-expressed in tumors relative to normal tissue, including lung, colon, breast and liver tumors. The drug exhibits a similar mechanism of action to the chemotherapeutic agent Mitomycin C, with greater activity against cells expressing high DTD and a more favorable safety profile.

"Pre-clinical work has shown RH1 to be a more efficient substrate for DTD than currently available agents," said David Ross, professor of toxicology and chairman, Dept. of pharmaceutical sciences at the University of Colorado. "This drug may offer a means to selectively target tumors expressing high levels of DTD."

RH1 is being evaluated for advanced solid tumors refractory to other chemotherapy regimens in an open label, phase I dose escalation 40-patient study chaired by Malcolm Ranson, director Derek Crowther Unit, Christie Hospital, Manchester, UK, the company said. The study would test the safety, tolerability and pharmacokinetics of escalating doses of the compound. DTD enzyme levels are being measured to correlate with drug efficacy. Recruitment began in September 2003 and is expected to complete in the second half of 2005, the company said.

Under agreement, Allos would make an up-front payment and a series of milestone payments, the company said.

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Applied Biosystems (NYSE: ABI) of Foster City, Calif., an **Applera Corp**. business, said it has expanded its collaboration with **Stanford University** and **University of Miami** to study genetic biomarkers for treatment response and survival in diffuse large B cell lymphoma.

While the previous study was based on samples from patients receiving standard chemotherapy, the second retrospective study would validate the predictive value of the six genes in a larger study using samples from patients who were treated with a combination of standard chemotherapy and Rituxan (rituximab) therapy, and whose outcomes are already known, the companies said.

A prospective study would follow patients from diagnosis in order to evaluate if the six genes can predict whether or not they respond to the combination of chemotherapy and Rituxan, and whether the biomarkers correctly identify those less likely to survive, the companies said.

While Rituxan is not indicated for DLBCL, it is being investigated for DLBCL due to its success with lymphoma and recent results that it may prolong survival in elderly patients, the companies said.

"By expanding our knowledge about the genetic biomarkers associated with diffuse large B cell lymphoma, we ultimately hope to provide clinicians with better tools to make treatment decisions," said Ronald Levy, professor of medicine, Stanford University Medical Center. "For example, if the model is validated and a patient is deemed unlikely to respond to currently available treatments, the patient may be a good candidate for alternative therapies under investigation."

In the initial DLBCL study, the researchers used a combination of microarrays, bioinformatics, real-time PCR and TaqMan Gene Expression Assays to narrow candidate genes to the six deemed most predictive of survival, the companies said. The current multi-site study would employ the Applied Biosystems TaqMan Low Density Array, a microfluidic card for real-time PCR that can screen hundreds to thousands of samples across a set of genes in order to determine which genes are expressed.

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Bavarian Nordic A/S of Copenhagen said it is establishing **BN ImmunoTherapeutics Inc**., a Palo Alto-based cancer vaccine research subsidiary engaged in research and development of vaccines for breast, prostate and colon cancers.

The company said it would utilize its patented MVA-BN vaccine vector in vaccine development programs.

"New data from an earlier study in melanoma cancer with a Bavarian Nordic trial vaccine based on the MVA-F6 vector expressing the melanoma antigen, (tyrosinase), demonstrate that the MVA-BN vector is able to break tolerance towards the self-antigen and induce a prolonged relevant therapeutic immune response over a period of more than a year," said Peter Wulff, president and CEO of Bavarian Nordic.

The US based cancer vaccine research organization would be led by Reiner Laus, CEO of BN ImmunoTherapeutics Inc. Laus is a former vice president of research & development at Dendreon Corp. of Seattle.

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ClinPro Inc. of Bound Brook, N.J., said it has formed a strategic alliance between its **Center for Oncology Research Management** and **GCP Clinical Studies Ltd**., a clinical research services and education programs provider of Israel.

GCP Clinical Studies would conduct the oncology clinical trials at the six largest cancer treatment centers in Israel, the company said.

"One of the biggest hurdles in clinical development of cancer drugs is the intense competition for patients to be able to participate in clinical trials - particularly in Phase I studies," says Howard Goldsweig, vice president of medical affairs at ClinPro. "To address the issue, ClinPro's Center for Oncology Research Management is pursuing a strategy of expanded access to qualified investigational sites outside the U.S. Among Israel's population of 6.7 million, there were 22,300 newly diagnosed cases of cancer recorded in 2001. Because of Israel's sophisticated clinical and research infrastructures, the U.S. FDA recognizes clinical trial data contributed by Israeli investigators."

GCP Clinical Studies works in collaboration with the global Association of Clinical Research Professionals, the Israeli Ministry of Health and the Israeli Medical Association, the company said. The research divisions provide full range of clinical research services from phase I to phase IV as well as post marketing and drug surveillance studies.

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Infinity Pharmaceuticals Inc. of Cambridge, Mass., said it has entered into a small molecule collaborative agreement with **Novartis AG** (NYSE: NVS).

Under the agreement, Novartis has made an equity investment in Infinity and would pay additional fees expected to exceed $10 million over the course of the two-year agreement, the company said. The Novartis Venture Fund has previously invested in Infinity.

"The natural product-like structures available through Infinity's established chemistry capabilities have a high likelihood of success in phenotypic approaches to drug discovery," Scott Biller, vice president and head of

global discovery chemistry for the Novartis Institutes for BioMedical Research, the research division of Novartis. "Infinity has an exceptionally robust platform for synthesizing diverse compounds and we look forward to using this asset to jointly design novel collections."

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Ligand Pharmaceuticals (Nasdaq: LGND) of San Diego said it has exercised the first option with **Eli Lilly and Co.** (NYSE: LLY) to buy down a portion of the royalties payable to Lilly on sales of the cancer drug Ontak (denileukin diftitox) in the U.S.

Ligand said it recorded sales of $34.3 million for Ontak in calendar year 2003 and $25.9 million in the first three quarters of 2004.

Ligand said would make a one-time cash payment of $20 million to Lilly in exchange for elimination of the Ontak royalties due to Lilly on net sales in the U.S. in 2005, and a reduced reverse-tiered royalty scale on net sales in the U.S. thereafter above a certain threshold.

Under the agreement, Ligand and Lilly each have two options related to Ontak royalties. Ligand has an independent option exercisable in January 2005 and another independent option exercisable in April 2005 to buy down a portion of the Ontak royalty stream on net sales in the U.S. for a total consideration of $33 million. Lilly has options in 2005 to trigger the same royalty buydown on Ligand's part for a total consideration of up to $37 million, depending on whether Ligand has exercised one or both of its options and Ontak has achieved certain sales levels, the companies said. Ligand has now exercised the first option under the agreement. The second option in April 2005 provides that Ligand may make a one-time cash payment of $13 million in exchange for the elimination of the Ontak royalties due to Lilly on net sales in the U.S. in 2006 and a reduced reverse-tiered royalty scale thereafter. If both Ligand options are exercised, Ligand would make total payments of $33 million for elimination of all royalty payments due on U.S. sales through year-end 2006 and elimination of all royalties on U.S. sales of $38 million or less going forward. Thereafter, beginning in 2007, Ligand would pay royalties to Lilly on a reverse-tiered scale (from 20 percent to 10 percent) only on annual U.S. sales in excess of $38 million for the minimum tier and in excess of $72 million for the maximum tier threshold for the remaining patent life (through 2014).

Ontak was approved in 1999 for persistent or recurrent cutaneous T-cell lymphoma where malignant cells express the p55 (CD25) component of the IL2 receptor, the companies said. The drug has been or is being tested in phase II trials for chronic lymphocytic leukemia, peripheral T-cell lymphoma, B-cell non-Hodgkin's lymphoma, non-small cell lung cancer, and graft-versus-host disease, the companies said.

In another development, **Ligand** and **TAP Pharmaceutical Products Inc.** of Lake Forest, Ill., said they would extend their research collaboration on selective androgen receptor modulators through June 2006.

The TAP-Ligand collaboration, which began in 2001, already has SARM molecules in advanced preclinical development for androgen-related diseases and disorders, including LGD2941 which is targeted for an IND filing in the first half of 2005, the companies said.

Under the agreement, TAP has been granted exclusive worldwide rights to manufacture, develop, and sell any products resulting from the collaboration in its field, including treatment and prevention of hypogonadism, male and female sexual dysfunction, female and male osteoporosis, frailty, male hormonal therapy and other indications not retained by Ligand, the companies said. Ligand may receive $3.4 million during 2005 in collaborative revenue and up to $44 million in research funding and milestones. Ligand may also receive up to double-digit royalties as compounds are developed and commercialized.

Ligand retains certain rights in the androgen receptor field, specifically prostate cancer, benign prostatic hyperplasia, acne, and hirsutism, the companies said. The company recently exercised its option to select one compound and a back-up for development, LG 123303 and LG 123129, which are not being developed by TAP in its field. TAP retains certain royalty rights and an option to negotiate to co-develop and co-promote such compounds with Ligand up to the end of phase II development.

TAP Pharmaceutical Products Inc., is a joint venture between Abbott of Abbott Park, Ill., and Takeda Pharmaceutical Co. Ltd.of Osaka, Japan.

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Locus Pharmaceuticals Inc. of Blue Bell, Penn., said it has entered into a cooperative research and development agreement with **NCI** to develop anti-cancer therapies using the Locus proprietary, fragment-based, computational technology.

The CRADA focuses on heat shock protein 90, because of its pathophysiological role in cancer and other cell proliferative diseases and disorders, the company said.

Under the agreement, Locus said it would create one or more series of molecules in silico designed

to have high specific affinity for Hsp90. NCI would then conduct preclinical studies on the synthesized compounds to identify those for clinical study. Locus said it has a first option to an exclusive license on any inventions resulting from the collaboration.

Hsp90 client proteins include a number of cancer-relevant targets such as the kinases Bcr-Abl, Raf-1, and Src, mutated p53, ErbB2, and the steroid hormone receptors. W. Douglas Figg, senior investigator and head of the Molecular Pharmacology Section and the Clinical Pharmacology Section at the NIH Center for Cancer Research, and Leonard Neckers, senior investigator of the Urologic Oncology Branch, are the principal investigators for NCI, the company said.

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Oxxon Therapeutics Inc. of Boston said it has licensed exclusive worldwide rights to the **Xenova Group plc** (Nasdaq: DISC-HSV and DISC-GM-CSF vector platforms to develop preventative and therapeutic products for cancers and chronic infectious diseases.

DISC-GM-CSF, used as a stand-alone product, has been tested in oncology indications including a dose-ranging phase I trial for melanoma, the company said.

The agreement includes use of the vectors both as part of priming and boosting regimens or as stand-alone products, the company said. Under the agreement, Xenova would receive a staged up-front fee, milestones and royalties on sales of products.

"Oxxon is building an immunotherapeutic pipeline through its proprietary PrimeBoost approach, a strategy that delivers disease antigens with two different, non-replicating vectors," said Deirdre Gillespie, president and CEO of Oxxon. "DISC-HSV and DISC-GM-CSF provide a new, versatile antigen delivery platforms that we can incorporate rapidly in new product candidates. Both vectors have produced potent immune responses in a number of models and have been demonstrated to be safe in humans. In addition, Xenova has developed an advanced manufacturing process for them."

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Sanofi-Aventis (EURONEXT: SAN and NYSE: SNY) said it has reaffirmed its commitment to develop the VEGF Trap in oncology in collaboration with **Regeneron Pharmaceuticals Inc**. (Nasdaq: REGN) of Tarrytown, N.Y., following a review of the Vascular Endothelial Growth Factor Trap program.

The companies said they would evaluate the VEGF Trap in a variety of cancer types, both in single-agent studies and in combination with chemotherapy. Sanofi-aventis also announced that Regeneron has earned a $25 million clinical development milestone payment.

"This is an important partnership for Sanofi-Aventis and we continue to believe that the blockage of VEGF is one of the most innovative approaches to targeted cancer therapy," said Marc Cluzel, vice president, international development, sciences & medical affairs of Sanofi-Aventis.

In addition, the companies said they have agreed that the exclusive right to develop and commercialize the VEGF Trap for eye diseases through local delivery systems reverts today to Regeneron. The collaboration would not currently pursue systemic delivery for eye disease.

In connection with the agreement, Sanofi-aventis said it would make a one-time, final payment to Regeneron of $25 million of which 50 percent is repayable to Sanofi-aventis following commercialization of the VEGF Trap.

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Serono (Virt-X: SEO and NYSE: SRA) of Geneva, Switzerland, and **CancerVax Corp**. (Nasdaq: CNVX) of Carlsbad, Calif., said they have entered into a worldwide collaboration for the development and commercialization of Canvaxin, an investigational specific active immunotherapy product advanced-stage melanoma.

The product is in two international, multi-center phase III trials for stage III and stage IV melanoma, the companies said.

Under the agreement, the companies said they would share equally the costs of developing the product and seeking regulatory approvals.

The companies also said they would co-promote Canvaxin in the U.S. and share expenses and profits on a 50/50 basis. Outside the U.S., Serono would have the exclusive right to commercialize the product and would pay royalties to CancerVax based on its sales of the product. Initially, CancerVax would manufacture Canvaxin for supply throughout the world. Serono could establish a second manufacturing site for Canvaxin, to supply primarily markets outside the U.S.

CancerVax said it would receive an initial cash payment of $37 million, comprised of $25 million in upfront signing fees and $12 million for the purchase of 1 million shares of CancerVax common stock. CancerVax could receive up to $253 million in additional payments linked to the achievement of development, regulatory and commercial milestones, the companies said. The element of the milestone payments relating to the receipt of regulatory approvals through to marketing Canvaxin solely in stage III and stage IV melanoma in the U.S. and the EU could amount to $100 million.