THE CANCER LETTER

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NCI Budget: A "Yes" For One Item Means A "No" To Something Else, Director Says

NCI will have to cut its programs as it adjusts to slowed growth in appropriations, Institute Director Andrew von Eschenbach said to the National Cancer Advisory Board last week.

"We have to, whenever we say 'Yes' to something, by definition, say 'No' to something else," von Eschenbach said Feb. 18, defending his recent decision to carve 5 percent out of the Institute's operating budget to create a reserve fund.

"The 'No' has to be as strategic as the 'Yes,'" he continued. "What we don't do has to be given careful thought and deliberation, as well as what we do do."

Mandatory cuts imposed by Congress and NIH, and funding

(Continued to page 2)

In Brief:

Horning Elected ASCO President-Elect; Five ASCO Members Named To Board

SANDRA HORNING was elected president-elect of the American Society of Clinical Oncology and will begin her term on June 8, during the society's 40th annual meeting in New Orleans. Horning, an ASCO member since 1983, is a professor of medicine in the Divisions of Medical Oncology and Blood and Marrow Transplantation at Stanford University. She is chairwoman of the Lymphoma Committee of the Eastern Cooperative Oncology Group, and is the project leader for NCI-sponsored research in Hodgkin's disease and non-Hodgkin's lymphoma. Horning served on the FDA Oncologic Drugs Advisory Committee, the NCI Leukemia, Lymphoma, and Myeloma Progress Review Group, and the NIH Clinical Oncology Study Section. She is a member of the advisory board for the Lymphoma Research Foundation and has participated in developing guidelines for lymphoma and Hodgkin's disease for the National Comprehensive Cancer Network. . . . **ASCO ELECTED** five new board members who begin three-year terms in June: **S. Gail Eckhardt**, professor of medicine, University of Colorado Health Sciences Center; **Hyman Muss**, professor of medicine, University of Vermont and a member of the Vermont Cancer Center; **Bruce Minsky**, vice chairman, Radiation Oncology and chairman of Quality Assessment at Memorial Sloan-Kettering Cancer Center; **Peter Eisenberg**, a community oncologist with California Cancer Care, of Greenbrae, Calif.; and **Nagahiro Saijo**, director of the Medical Oncology Division of the National Cancer Center Hospital in Tokyo and chairman of the Japanese Clinical Oncology

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Budget Notwithstanding, Cancer Research Is "Blessed"

(Continued from page 1)

commitments to grants awarded in previous years left NCI with little money to support new initiatives, von Eschenbach said.

"We have to be able to grow new opportunities and new resources," he said. "We have to be able to accomplish and achieve strategic priorities. Unlike years ago, we cannot do that with new money coming in by virtue of the appropriation.

"We have to do that by redeployment of the resources already in place," he said.

For fiscal 2004, NCI received an appropriation of $4.77 billion, an increase of $178 million, or 3.9 percent, over fiscal 2003. The bill included cuts totaling $31 million. NCI also had to contribute $16 million to NIH for the Roadmap initiatives. Research project grants awarded in previous years will require $113 million of what's left.

The Institute ended up with only about $18 million in new, uncommitted funds, sources said. In his remarks to the NCAB, von Eschenbach indicated that even that money has been obligated.

"The fact of the matter is, we start the year almost in a deficit," he said. "With what we had to provide to other commitments in place, we had essentially no money to do strategic initiatives."

The initiatives that von Eschenbach envisions require "very aggressive, very demanding, very extensive strategic planning and business planning," he said.

The 5 percent cut will create a reserve of about $70 million to $90 million (**The Cancer Letter**, Feb. 13).

NCI division directors have been "passionate" in "guarding and protecting their portfolio" from cuts, von Eschenbach said. "But we need to be working across the strategy that guides and directs the entire enterprise," he said.

"We will be redeploying resources at times from one part of the organization to another in order to be able to meet our strategic opportunities and strategic priorities," von Eschenbach said.

Next fiscal year appears unlikely to provide relief. The fiscal 2005 budget request President Bush submitted to Congress earlier this month includes $4.87 billion for NCI, an increase of $134 million, or 2.8 percent (**The Cancer Letter**, Feb. 6).

NCI's "guiding principle" for the fiscal 2005 budget will be to protect investigator-initiated research, von Eschenbach said.

This year, NCI plans to maintain a 20-percent payline for research project grants, but will impose an 18 percent cut on new grants.

"We have budget challenges," von Eschenbach said. "But we have unbelievable opportunities."

In remarks similar to those he has made in other venues, von Eschenbach took an optimistic view of the cancer research budget.

"There has never been as much money invested in cancer research as there is right now, at this moment," he said. "We've never had as much in the way of resources to work with.

"We've never had as many people--committed, talented people--working in cancer research as we have right now, today," he said. "We've never had the strength and the power of institutions and organization as great as they are today.

"We are blessed," von Eschenbach said.

"Whether we are talking about cancer centers, or whether we are talking about organizations like AACR, ASCO, American Cancer Society, and on and on. Whether we are talking about advocacy groups, etc.

"We have never been stronger. We have never had more opportunity.

"This Institute is committed to focus on that opportunity, using those strengths, and assure that by 2015, no one in this country suffers or dies as a result of cancer," he said.

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The Challenge of An Aging Population

In half the time between now and 2015, an aging U.S. population will severely test the cancer-care system, President's Cancer Panel member Margaret Kripke said to the NCAB.

"In six years, the first cohort of Baby Boomers will reach the age of 65, and since this population has 59 percent of all cancer diagnoses, and 70 percent of all cancer deaths occur in the population of 65 and over, this represents an enormous challenge both to health care systems and to cancer centers and cancer treatment communities in general," said Kripke, executive vice president and chief academic officer of M.D. Anderson Cancer Center.

"Cancer diagnoses and cancer treatment are complicated in this population by comorbidities, which often obscure diagnosis and also complicates treatment," she said. "We are all concerned that neither cancer centers nor the National Cancer Program is really prepared for what will be a deluge of cancer cases and health-care needs in this population."

Over the next year, one of the questions the panel plans to study is, "What is the role of the academic medical centers in helping to translate research at every step, but also, what are the best mechanisms for moving research out into the communities," Kripke said.

NCAB Chairman John Niederhuber asked the panel to consider how community-based centers that are not NCI-designated centers can be incorporated into the National Cancer Program. "They tell me they feel very disconnected with what's going on in Washington," said Niederhuber, professor of oncology and surgery, University of Wisconsin-Madison. "This is a resource that maybe we need if we are going to address the needs of an aging population. I don't think we know how to make them feel a part of what we are doing."

Panel Chairman LaSalle Leffall Jr. said the group plans to address the issue in a future meeting. "We plan to re-connect them if they feel disconnected," said Leffall, the Charles R. Drew Professor of Surgery at Howard University College of Medicine.

NCI needs to begin studying the problem of the aging population, von Eschenbach said.

"We are looking at this as a systems problem, and looking forward to creating linkages [between NCI and other organizations]," he said. "We also recognize the critical importance that cancer centers—both the NCI-designated as well as community cancer centers—can play in this particular role.

"One of the implications of 2015 is that we had 3 million cancer survivors in 1971, we have 10 million today," von Eschenbach said. "By 2015, there will be a lot of people who have experienced cancer and who are alive and well, and we need to be prepared for that."

Over the past year, the Cancer Panel held public forums on cancer survivorship. The panel's reports are posted at http://deainfo.nci.nih.gov/ADVISORY/pcp/statment.htm.

"Progress Is Only Possible Because of People"

In the next year, NCI plans to emphasize staff development, von Eschenbach said to the NCAB.

At last year's "all hands" NCI staff meeting, von Eschenbach said he presented the theme of "Progress With A Purpose" and "the importance of eliminating the suffering and death due to cancer," he said to the NCAB.

"This year, it was my great privilege to meet with [staff] and share with them the fact that it is progress with a purpose, but progress is only possible because of people," von Eschenbach said.

"It is a human endeavor, and it is the incredible people within this organization and throughout this entire cancer enterprise that are really, truly making it feasible and reasonable to imagine and envision a country, a world, in which no one suffers and dies due to cancer."

NCI will have a "reduction in force" this year, he said, but did not provide further details. The Institute has to cut about 100 of its full-time equivalents (**The Cancer Letter**, Feb. 13).

"We have many challenges along that line, and I have again the blessing of many talented people to work with to be able to manage and deal with some of those challenges," von Eschenbach said. "We are not only looking at the problems, but we are also looking at the opportunities."

NCI plans to recognize staff members who "go the extra mile" by presenting them with the Director's Gold Star award, von Eschenbach said.

He also plans to enhance opportunities for career development, he said. As an example, in the past year, division directors have participated in "formal management programs" that involve "coaching an instruction with regard to managing and dealing with the challenges that come with being a leader in a complex organization like this."

Another major area of emphasis will be diversity, he said.

"We want to make certain that our workforce is respecting, valuing, and promoting diversity," he said. "I mean diversity in every possible meaning of that

word. Diversity that transcends racial, cultural, ethnic differences, but also differences in skill sets, talents, abilities, backgrounds, points of view."

FDA News:

McClellan Nominated To Head Medicare, Medicaid Center

President George W. Bush has nominated FDA Commissioner Mark McClellan for the post of administrator of the Centers for Medicare and Medicaid Services.

If anything, the new job would make McClellan a more important player in oncology. This year's reforms have expanded Medicare's mandate to oversight of the new Medicare prescription drug benefit.

Also, Medicare is grappling with questions of cost of new treatments, regulating reimbursement for office-based oncologists, and considering changes in reimbursement for off-label use of cancer drugs.

After taking FDA job in November 2002, McClellan sought to streamline the agency's review mechanisms. As he attempted to shorten review time, he focused attention on a greater problem: the slowing down of medical research and the barriers to innovation.

Invited recently to speak at NCI Director Andrew von Eschenbach's lecture series designed to reflect the pursuit of the "2015 Goal," McClellan was far from triumphalist. Instead, he spoke about formidable challenges to drug development (**The Cancer Letter**, Feb. 6, 2004).

At FDA, McClellan will be replaced by Deputy Commissioner Lester Crawford, who will become the acting commissioner. Crawford, a veterinarian, held the job for nine months prior to McClellan's appointment.

In a memorandum Feb. 20, McClellan said the agency would streamline its "internal lines of communication." The changes include:

--"We will be going to a three Deputy Commissioner system on an acting basis until further notice," Crawford wrote. Janet Woodcock was named Deputy Commissioner for Operations. Murray Lumpkin became Deputy Commissioner for Special Programs, and Amit Sachdev became Deputy Commissioner for Policy.

--Mary-Lacey Reuther was named Director of Departmental and Interdepartmental Relations, coordinating FDA interactions with HHS and other departments down to the agency level.

--Scott Gottlieb was appointed Director of Medical Policy Development, coordinating Office of Commissioner liaison with the Centers for Biologics Evaluation and Research, Medical Devices and Radiological Health and Drug Evaluation and Research.

--Susan Bond was appointed Director of Scientific Policy Development, coordinating Office of Commissioner liaison with the Center for Food Safety and Applied Nutrition, the National Center for Toxicological Research, and the Center for Veterinary Medicine.

"The impressive Strategic Plan and Goals that we have in place will not change and will serve as the collective blueprint for the remainder of this Administration," Crawford wrote. "We are doing well in terms of public approval and concrete accomplishments."

McClellan was expected to have little trouble getting Senate confirmation for the CMS job, Washington sources said.

FDA To Refer False Statements By Regulated Firms To SEC

FDA said it is establishing a centralized procedure for referral to the Securities and Exchange Commission of statements by FDA-regulated firms that may be false or misleading.

The limits on the ability of FDA to report false representations to SEC became the focus of Congressional attention two years ago, during the controversy that surrounded ImClone's representations about its application for the approval of Erbitux.

"The SEC and its staff have primary responsibility for enforcing the rules requiring truth in the securities market, which is essential for its proper functioning," said FDA Commissioner Mark McClellan. "Unfortunately, companies sometimes violate the public trust by issuing false or misleading statements about FDA-related issues, such as the progress of FDA's pre-market review. When we identify suspected misstatements, we have a new process to bring them to the attention of the SEC staff as quickly and efficiently as possible."

Under the new referral procedure, any FDA employee who believes a publicly held, FDA-regulated firm has made a false or misleading statement to the investment public concerning a matter within FDA's authority can initiate a process for referring the matter to the SEC Division of Enforcement.

FDA employees will not be expected routinely to police statements by publicly held, FDA-regulated companies, the agency said. However, FDA can be in a position to identify statements that may be of interest

to the SEC and its staff, and FDA employees will have a centralized procedure to make SEC referrals if, in the normal course of their activities, they come to believe that a company may have made a false or misleading statement to the investing public, the agencies said.

In addition to establishing the referral procedure, FDA is implementing the following administrative measures to improve the assistance it provides to SEC and its staff:

--FDA Contacts. FDA has identified a liaison officer as well as specific contacts within the agency,s principal operational components for the SEC and its staff to use in requesting information from FDA.

--Training. FDA is working with the SEC and its staff to identify opportunities for the two agencies to engage in training in areas of mutual interest.

--Electronic Communication. FDA will use electronic media when possible, e.g., to provide information or technical support to the SEC or its staff, receive requests from the SEC for non-public information, and review statements in annual reports and other SEC filings made by FDA-regulated firms.

--Non-Public Records/Information. FDA will provide specified FDA employees a blanket authorization to enable them to share non-public information with the SEC or its staff, rather than executing such authorizations on a case-by-case basis. FDA and SEC staff have agreed to continue identifying additional measures that might be implemented to improve the process by which FDA shares non-public information with the SEC and its staff in accordance with FDA's laws and procedures.

Professional Societies:

Medicare Coverage, Quality Of Care, Top ASCO Priorities

While the top legislative priority for clinical oncologists this year will be to seek a freeze in Medicare cuts for oncology drug reimbursement, officials of the American Society of Clinical Oncology discussed several other topics of interest to oncologists in a meeting with reporters earlier this month.

In an election year, the shorter legislative cycle "is going to be a challenge," said Deborah Kamin, senior director for ASCO's Cancer Policy and Clinical Affairs department. "There is always an opportunity to do something, to create the concern and the momentum," she said.

The group's policy priorities for 2004 include:

--National Initiative on Cancer Care Quality: ASCO is conducting the first large-scale study to assess the feasibility of building and implementing a national system to monitor cancer care quality. The study will be released at the annual meeting in June and will be followed by a series of public meetings.

--Improving Palliative and End-of-Life Care: ASCO will continue its emphasis on improving professional education programs to ensure that training on palliative care issues becomes an essential element of the curricula for medical professionals.

--Medicare Coverage of Oral Chemotherapy: The recently enacted Medicare prescription drug bill provides for a demonstration project for Medicare coverage of oral chemotherapy drugs that do not have an infusion equivalent, coverage that had previously been denied under Medicare. The demonstration project is limited to $500 million and 50,000 people, which also includes coverage of self-injectible drugs for multiple sclerosis and rheumatoid arthritis. ASCO plans to work with CMS and Congress to determine what cancers the demonstration projects should address and how to ensure that a larger number of people with cancer can benefit from the program.

--Medicare Reimbursement for Off-Label Uses of Cancer Drugs: ASCO has asked CMS to refrain from restricting coverage of cancer drugs used for off-label uses.

--Medicare Reimbursement for Cancer Treatment: ASCO supports a legislative position that would maintain total Medicare payments for chemotherapy and related services at 2004 levels for a two-year period (**The Cancer Letter**, Feb. 20).

--Increasing Patient Access to Clinical Trials: ASCO is surveying oncology practices to asses their awareness of and attitude toward state legislation addressing reimbursement of routine care costs associated with clinical trials. Among states that have clinical trial laws, ASCO is assessing physicians' familiarity with the law and whether it has been helpful in their ability to enroll patients in clinical trials. For states without such statutes, ASCO is assessing the status of clinical trials awareness and access. Results of the survey will be reported at the annual meeting. Also, ASCO is sponsoring a workshop this fall on clinical trials participation for community oncologists.

--Enhancing Clinical Research Oversight and Ensuring Patient Safety: ASCO is committed to working with research sponsors, clinical investigators, and policy makers to improve the effectiveness and efficiency of the clinical research oversight system.

--Commission to Reduce Tobacco Use: ASCO is working to establish an independent commission to

study the tobacco problem in all of its dimensions—social, medical, legal, and economic, both domestically and globally. The commission would be charged with formulating recommendations on how best to address these issues to obtain the goals of immediate reductions and eventual elimination of tobacco use.

--Ensuring Non-Discrimination for People with a Genetic History of Cancer: ASCO supports a federal law to prohibit discrimination by health insurers and employers based on an individual's inherited susceptibility to cancer and other diseases. Protections should apply to those with all types of insurance, as well as the uninsured.

NIH News:

NIH Conflict of Interest Panel Appointed, To Meet March 1

NIH Blue Ribbon Panel on Conflict of Interest Policies will hold its first meeting March 1-2.

The panel's charge is to review and make recommendations for improving the existing NIH rules regarding financial conflict of interest of NIH staff . The panel will provide recommendations to the Advisory Committee to the Director.

Bruce Alberts, president of the National Academy of Sciences, and Norman Augustine, chairman of the Executive Committee of the Lockheed Martin Corp., are co-chairmen of the panel, which is a working group of the Advisory Committee to the NIH Director.

The panel members are: Christine Cassel, president, American Board of Internal Medicine and member of the ACD; Thomas Murray, president, The Hastings Center; Phillip Pizzo, dean, School of Medicine, Stanford University; Stephen Potts, chairman, ERC Fellows Program, Ethics Resource Center; Dorothy Robinson, vice president and general counsel, Yale University; Lawrence Sadwin, president, Lifestyle Security, and member of the NIH Council of Public Representatives; James Siedow, vice provost for research and professor of biology, Duke University; and Reed Tuckson, senior vice president, Consumer Health and Medical Care Advancement, UnitedHealth Group.

"We have assembled leading experts on institutional management and ethics to provide an impartial review of NIH's consulting practices and provide recommendations to my advisory committee for systemic changes to ensure NIH ethics policies and procedures regarding outside activities are fully transparent to the public," NIH Director Elias Zerhouni said.

The meeting will be open to the public and will be held at NIH Building 31C, Conference Room 10.

Funding Opportunities:

RFA Available

RFA-CA-04-016: NCI Career Development Award for Quantitative Scientists

Letter of Intent Receipt Date: March 22, 2004

Application Receipt Date: April 20, 2004

The RFA is soliciting applications from doctoral-level quantitative scientists who wish to become cancer researchers as independent investigators and/or as leaders or co-leaders of interdisciplinary cancer research teams. Examples of scientific and technical backgrounds considered appropriate, but not all inclusive, for this award are as follows: physics, mathematics, computer science, imaging science, informatics, statistics, economics, chemistry, engineering, and nanotechnology. The award provides up to 5 years of salary and research support for a mentored research career development experience in biomedical cancer research. The RFA will use the NIH K25 career development award mechanism. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-04-016.html.

Inquiries: Lester Gorelic, Cancer Training Branch, phone 301-496-8580; e-mail gorelicl@mail.nih.gov.

CA-05-014: Community Clinical Oncology Program

This Community Clinical Oncology Program RFA seeks to strengthen the CCOP by: 1) continuing the program as a vehicle for supporting community participation in cancer treatment and prevention and control clinical trials through research bases (clinical cooperative groups and cancer centers supported by NCI); 2) expanding and strengthening the cancer prevention and control research effort; 3) utilizing the CCOP network for conducting NCI-assisted cancer prevention and control research; and 4) evaluating, on a continuing basis, CCOP performance and its impact in the community.

Participating CCOPs will be required to enter participants onto NCI-approved cancer treatment and prevention and control clinical trials through the research base(s) with which the CCOP is affiliated. CCOPs may contact NCI program staff directly for assistance and participation in selected cancer prevention and control protocols. CCOP performance will be evaluated on a continuing basis by the NCI program director.

CCOP applicants must demonstrate the potential for accessing appropriate cancer patients/participants within their communities for participation in cancer treatment and prevention and control protocols provided by their research bases.

Contact: Lori Minasian, Community Oncology and Prevention Trials Research Group, phone: 301-496-8541, e-mail: lm145a@nih.gov.

Program Announcement

Paul Calabresi Award For Clinical Oncology

This PAR replaces the NCI "Institutional Clinical

Oncology Research Career Development (K12) Program" (PAR-CA-030-083) with the "Paul Calabresi Award for Clinical Oncology (K12)" or PCACO.

The purpose of the PCACO is to increase the number of medical doctors (M.D.'s, D.O.'s), doctorally-degreed nurses and basic scientists (P.h.D.'s, D.V.M.'s or equivalent) who are highly motivated and trained to: 1) perform clinical oncology therapeutic research that develops and tests scientific hypotheses based on fundamental and clinical research findings; 2) design and test hypothesis-based clinical therapeutic protocols and adjunct biological analyses and for clinician candidates administer all phases (i.e., pilot/Phase I, Phase II, and Phase III) of cancer therapeutic clinical trials, and (3) conduct cancer therapeutic research in team research settings in which basic and clinical scientists collaborate and interact to expedite the translation of basic research discoveries into patient-oriented therapeutic cancer research. The PCACO is not intended to train laboratory-based scientists whose research will emphasize the use of animal or other model systems.

Awards for up to $800,000 annually (clinician candidates only) or up to $1,100,000 annually (clinician and basic scientists candidates, with the ratio of clinician basic science candidates being greater than or equal to two) in direct costs are made to institutions for up to 5 years, and are renewable. Appointments of candidates to the Program should be for a minimum of 2 years. As long as a K12 has been renewed, individual clinician candidates can be supported for up to 7 years.

The K12 Program must involve staff and clinical candidates representing at least two clinical oncology disciplines. The Program should include didactic, clinical research, and basic research core components. All candidates graduating from the Program must complete core didactic, clinical, and basic research core requirements either directly or through combination with their past training experience. The K12 Program must use an Advisory Committee to provide an oversight function and annual evaluation of the Program as a whole.

Clinician candidates must currently be physicians holding the M.D. or D.O. degrees or nurses with a Ph.D. degree; and must have completed the necessary clinical training (i.e., completed residency and are board eligible) to engage in clinical oncology research. Basic science candidates must have doctoral-level degrees (e.g., Ph.D., D.V.M.) or the equivalent, a minimum of 2 years of postdoctoral research training, and a total basic research experience that is clearly preparatory (e.g., experience with animal models or preclinical research) for devoting a career to human therapeutic cancer research.

Candidates must be able to spend a minimum of 75 percent effort conducting research and research career development which includes all relevant didactic activities during the period of the award. The Program provides up to $75,000 annually for salary and up to $25,000 annually for research-related costs for each trainee. The Program also provides up to 10 percent of the Principal Investigator/Program Leader's salary plus fringe benefits, some partial salary plus fringe benefits for a dedicated administrator, and up to $5,000 total per annum for each mentor may be derived from this grant, as long as these costs are approved by peer reviewers. Minimal costs can be allocated for advertising and recruitment in order to attract the best candidates nationally.

Contact: Lester Gorelic, Cancer Training Branch, phone: 301-496-8580, e-mail: gorelicl@mail.nih.gov.

Office of Research Integrity:

Postdoc Falsified Research In Papers Submitted to JCB

Bernd Hoffmann, a former postdoctoral fellow and adjunct assistant professor, Department of Pharmacology, University of Medicine and Dentistry of New Jersey, was found to have engaged in scientific misconduct in research supported by NIH, according to the HHS Office of Research Integrity.

The finding was based on two investigation reports by UMDNJ into NIH grant 2 R01 GM052309-05. Hoffmann engaged in scientific misconduct by falsifying and fabricating research data in a manuscript entitled "LIS1/NUDF and CLIP-170 are required for dynein-mediated vesicle transport on microtubules" that had been submitted to the Journal of Cell Biology, but was withdrawn before publication.

Hoffmann has agreed to exclude himself from contracting or subcontracting with the federal government for a period of three years, and drafted a letter of retraction of a JCB paper published at 276:38877-38884, 2001.

In Brief:

Dennis Slamon Receives ACS Medal of Honor For Research

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Group. . . . **TWO ASCO MEMBERS** were elected to three-year terms on the Nominating Committee: **James Abbruzzese**, the M.G. and Lillie A. Johnson Chair for Cancer Treatment and Research, professor of medicine, and chairman of the Department of Gastrointestinal Medical Oncology at University of Texas M.D. Anderson Cancer Center; and **Joyce O'Shaughnessy**, a medical oncologist with Texas Oncology, PA, U.S. Oncology at Baylor-Sammons Cancer Center. . . . **DENNIS SLAMON**, known for his research leading to the development of Herceptin, received the Medal of Honor award for clinical research from the American Cancer Society on Feb. 28. He is director of clinical/

translational research at the Jonsson Cancer Center at University of California, Los Angeles, and director of the Revlon/UCLA Women's Cancer Research Program. . . . **STEPHEN JAMES** has been appointed director of the Division of Digestive Diseases and Nutrition at National Institute of Diabetes and Digestive and Kidney Diseases. James has served as deputy director of the division since 2001. After a gastroenterology fellowship at the University of Maryland, James came to the NIH in 1977 as a medical staff fellow in the Liver Diseases Section of NIDDK and began studies on the immunology of liver disease. He furthered his training in immunology at NCI in the early 1980s. . . . **ASCO GERIATRIC ONCOLOGY** medical training programs will be established through a seed grant from the John A. Hartford Foundation. **Charles Balch**, ASCO executive vice president and CEO, and **John Bennett**, professor of medicine, University of Rochester Medical Center, serve as co-principal investigators. Programs funded by the grants include: Boston Medical Center; Duke University Medical Center; Johns Hopkins University School of Medicine; Northwestern University; University of California, Los Angeles; University of Chicago; University of Colorado Health Sciences Center; University of Michigan Medical Center; University of Rochester; and University of Texas, San Antonio. . . . **LYMPHOMA RESEARCH FOUNDATION** awarded $1,065,000 in research grants to investigators at eight U.S. institutions. The 2004 grants were awarded to: **Mei Kong**, Abramson Family Cancer Research Institute, University of Pennsylvania; **Jean Marie Bruey**, Burnham Institute, La Jolla; **Andreas Kruger**, Dana-Farber Cancer Institute; **John Pagel**, Fred Hutchinson Cancer Research Center; **Masahiro Yoshimura** Harvard University; **Michaela Liedtke**, Memorial Sloan-Kettering Cancer Center; **Paul Norman**, Stanford University School of Medicine; **Alice Fan**, Stanford University School of Medicine; and **Matthew Glenn**, Yale University. . . . **ROBERT SATCHER,** of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, received a $365,400 grant from the Robert Wood Johnson Foundation through its Harold Amos Medical Faculty Development Program for skeletal metastasis in prostate cancer. Satcher is assistant professor, Department of Orthopedic Surgery at the Feinberg School of Medicine, Northwestern University and adjunct professor, Department of Biomedical Engineering. He is also on staff at Children's Memorial Hospital and Northwestern Memorial Hospital.

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Business & Regulatory Report

Product Approvals & Applications:

FDA Approves Avastin For Use With 5-FU For Untreated Metastatic Colorectal Cancer

Genentech Inc. (NYSE: DNA) of South San Francisco announced FDA approval of Avastin (bevacizumab) to be used in combination with intravenous 5-fluorouracil-based chemotherapy as a treatment for patients with first-line-or previously untreated-metastatic cancer of the colon or rectum.

Avastin is the first FDA-approved therapy designed to inhibit angiogenesis. A 925-patient pivotal trial demonstrated a prolongation in the median survival of patients treated with Avastin plus the IFL (5-FU/

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Oncology Management:

NCCN Opens Leukemia Resource Line To Offer Physicians Expert Guidance

National Comprehensive Cancer Network of Jenkintown, Pa., has established a Leukemia Resource Line for physicians.

Expert guidance is available within one to two business days from members of the NCCN Acute Myeloid Leukemia Guidelines panel: Harry Erba, assistant professor, University of Michigan Comprehensive Cancer Center; Margaret O'Donnell, associate clinical director, Division of Hematology/Bone Marrow Transplantation, City of Hope Cancer Center; and Martin Tallman, director, Hematologic Malignancy Program, Robert H. Lurie Comprehensive Cancer Center of Northwestern University, the group said.

Physicians seeking guidance can call 1-888-469-NCCN (6226) or e-mail LeukemiaResource@nccn.org for feedback on diagnosing and treating leukemia patients, the group said.

* * *

American College of Obstetricians and Gynecologists and the **Society of Gynecologic Oncologists** published the first referral guidelines in 2002 for pelvic masses.

In the study of more than 1,000 women diagnosed with pelvic masses requiring surgery, a group of physicians found that when the guidelines were used, 94 percent of women with post-menopausal ovarian or other gynecologic cancers would have been appropriately referred to gynecologic oncologists for specialized treatment, the groups said.

The study involved a retrospective examination of women who had surgery for a pelvic mass between July 2000 and June 2001 at seven

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FDA Approves Two Drugs For Colon Cancer: Avastin, Erbitux

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Leucovorin/CPT-11) chemotherapy regimen by approximately five months, compared to patients treated with the IFL chemotherapy regimen alone (20.3 months versus 15.6 months). In addition, the study demonstrated an improvement in progression-free survival of more than four months (10.6 months in the Avastin/IFL arm compared to 6.4 months in the IFL-alone arm).

The survival and PFS results observed when Avastin is added to first-line chemotherapy are the longest ever reported in a randomized, phase III study of patients with metastatic colorectal cancer, the company said.

In the pivotal trial, the most serious adverse events that occurred with Avastin included gastrointestinal perforations and wound healing complications, which were uncommon, the company said. The most common severe adverse events in this trial included hypertension, which was managed with oral medications, nosebleeds and asymptomatic proteinuria. Adverse events observed in other trials with Avastin included hemorrhage, congestive heart failure and thromboembolism.

The Avastin Biologics License Application was submitted under the FDA's Fast Track program.

The Vascular Endothelial Growth Factor (VEGF), was discovered by Napoleone Ferrara, a scientist at Genentech, the company said. Ferrara and his team cloned VEGF, providing some of the first evidence that a specific angiogenic growth factor existed. This research was published in the journal *Science* in 1989. Ferrara then created a mouse antibody to this protein. In 1993, Ferrara and his team, in a study published in *Nature*, demonstrated that the antibody directed against VEGF could suppress angiogenesis and tumor growth in preclinical models, providing compelling evidence that VEGF can play a critical role in tumor growth. Clinical studies with a humanized version of the antibody, Avastin, began in 1997.

"Since the pivotal trial results were presented last year, I have had the privilege of meeting several patients who have received treatment with Avastin, and this has been the most rewarding part of watching a scientific theory progress from the lab to the clinic," said Ferrara. "The approval of Avastin is a testament to the many scientists both within Genentech and around the world who have worked tirelessly, even in the face of adversity and skepticism, to contribute to our understanding of angiogenesis and VEGF."

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ImClone Systems Inc. (Nasdaq: IMCL) and **Bristol-Myers Squibb Co**. (NYSE: BMY) said FDA approved Erbitux (cetuximab) for use in combination with irinotecan in the treatment of EGFR-expressing, metastatic colorectal cancer refractory to irinotecan-based chemotherapy.

Erbitux was also approved for use as a single agent for EGFR-expressing, metastatic colorectal cancer in patients intolerant to irinotecan-based chemotherapy.

The antibody was approved under the FDA accelerated approval program. Although treatment with Erbitux has not been shown to extend lives, it was shown to shrink tumors in some patients and delay tumor growth, especially when used as a combination treatment, the agency said.

The FDA submission included data from a randomized two-arm phase II trial conducted by Merck KGaA evaluating Erbitux as a single agent and the combination of Erbitux and irinotecan in 329 patients with EGFR-expressing metastatic colorectal cancer refractory to irinotecan-based chemotherapy.

The findings showed that Erbitux, given in combination with irinotecan (n=218), had an objective response rate of 22.9 percent, a median duration of response of 5.7 months and a median time to disease

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progression of 4.1 months, the companies said. Results of the Erbitux single agent treatment group (n=111) showed a 10.8 percent objective response rate, a median duration of response of 4.2 months and a median time to disease progression of 1.5 months.

The Merck studies revived the Erbitux application. In December 2001, FDA refused to file ImClone's NDA, stating that it was uninterpretable (**The Cancer Letter**, Jan. 4, 2002). FDA said the application couldn't be reviewed, because approximately half of the patients (94) studied had not failed the approved treatments for colon cancer; and important information about the safety and effectiveness of Erbitux in a portion of the remaining patients (102) was missing.

In the new request for approval on Aug. 14, 2003, ImClone submitted the results of Merck's trial as well as the results of the two studies. For the studies submitted in their original 2001 request for approval, ImClone collected substantial amounts of missing information from hospital records and other sources, FDA said.

Results from these single arm studies, which have been reanalyzed by ImClone and BMS, showed that Erbitux given in combination with irinotecan (n=138) had an objective response rate of 15 percent and a median duration of response of 6.5 months, FDA said. Results of the Erbitux single agent study (n=57) showed a 9 percent objective response rate and a median duration of response of 4.2 months.

"Cetuximab validates the concept that non-chemotherapeutic molecular drugs are active in the treatment of colorectal cancer," Howard Hochster, professor of medicine at the New York University School of Medicine, said in a statement. "It adds a new dimension in the treatment of this disease and allows oncologists new options for treating patients that have this disease when irinotecan-based chemotherapy is no longer effective or tolerated."

Two studies involving 2,000 patients are underway to assess the clinical benefits of treatment.

ImClone and BMS also said FDA has approved Lonza Biologics' manufacturing facility. Erbitux inventory previously produced at Lonza Biologics' facility will serve as supply for the initial demand for Erbitux.

ImClone withdrew its manufacturing facility (BB36) from the Chemistry, Manufacturing and Controls section of its Biologics License Application, and submitted a CMC supplemental BLA for licensure of the facility, FDA said.

Based on Prescription Drug User Fee Act guidelines, FDA has four months from the submission date to take action on the CMC supplemental BLA filing. The withdrawal and resubmission followed a request from the FDA for information on a larger group of patients treated with drug supplied from BB36 to confirm previously submitted safety data from that facility. This information has been collected from the company's phase II Erbitux single agent study of patients with EGFR-expressing refractory metastatic colorectal cancer (IMCL-0144). The CMC supplemental BLA includes the previously withdrawn BB36 CMC section, as well as information on the larger group of patients.

In June 2002, FDA authorized Erbitux manufactured at BB36 for investigational use, and the companies will continue to utilize this supply in ongoing and planned clinical trials. In addition, Swissmedic approved Erbitus manufactured at BB36 for commercial use in Switzerland in December 2003, in addition to a European manufacturing site (Boehringer Ingelheim).

Side effects of Erbitux include difficulty breathing and low blood pressure. Infrequent interstitial lung disease has been reported; however, it is difficult to determine if Erbitux caused ILD, FDA said. ILD occurs when the lung becomes stiff due to scarring of the tissue between the air sacs of the lungs.

Other more common side effects of Erbitux treatment include acne-like rash, dry skin, tiredness or weakness, fever, constipation, and abdominal pain, the administration said.

FDA also approved a test kit, manufactured by DakoCytomation California Inc., used to analyze a colon tissue sample. The kit detects a HER-1 protein that stimulates cancerous tissue cell growth. Presence of this protein indicates that a patient is eligible for colon cancer treatment with Erbitux, the agency said.

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Eli Lilly and Co. of Indianapolis (NYSE: LLY) said FDA has approved Alimta (pemetrexed disodium) for use with cisplatin for malignant pleural mesothelioma.

"Throughout the 1970s, '80s and really the '90s, we tried a host of different drugs, and most of them had virtually no effect on the cancer," said Nicholas Vogelzang, director of the Nevada Cancer Institute in Las Vegas, who led the global phase III trial evaluating Alimta/cisplatin while director of the

University of Chicago Cancer Research Center. "Alimta/cisplatin proved different."

Alimta is the first drug approved for this condition. About 2,000 new cases of mesothelioma are diagnosed in the U.S. each year. The disease is usually associated with a history of asbestos exposure.

The drug regimen was compared to cisplatin alone in 448 patients from 19 countries—the largest trial to date, the company said. Results showed overall survival was increased 30 percent (12.1 months for Alimta/cisplatin versus 9.3 months for cisplatin alone), and that 50.3 percent of patients treated with Alimta/cisplatin were alive a year later compared to 38.0 percent treated with cisplatin alone. Both the median and one-year rate of survival were statistically significant, the company said.

"There was an improvement in lung function on the Alimta/cisplatin arm compared to the cisplatin (or control) arm, " said Claude Denham, study co-investigator for US Oncology and medical oncologist with Texas Oncology in Dallas.

The hematolgoic and non-hematologic side effects associated with Alimta are neutropenia, thrombocytopenia, anemia, nausea, vomiting, fatigue, diarrhea, skin rash and pain, the company said. To reduce the severity of treatment-related toxicities, daily doses of folic acid and intramuscular injections of vitamin B12 are administered, the company said.

In Europe, Lilly said it has completed its submissions for Alimta with cisplatin for malignant pleural mesothelioma and single-agent Alimta in the second-line treatment of non-small cell lung cancer. Lilly said it has also submitted a new drug application to FDA for single-agent Alimta for second-line non-small cell lung cancer.

Orphan drugs are developed to treat rare diseases, that is, conditions that affect fewer than 200,000 people in the U.S. The Orphan Drug Act provides a seven-year period of exclusive marketing for the drug to the first sponsor who obtains marketing approval for a designated orphan drug.

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Lifeline BioTechnologies Inc. (OTC: LBTT) of Reno, Nev., said the company had completed the required documentation for compliance and FDA clearance of its breast microendoscope.

"This is a real milestone for us and we are quite excited about our upcoming U.S. as well as our European market entry with this product," Jonathan Reeves, vice president of operations at Lifeline. "It has been a long and tedious process for us. Having worked for well over a year with outside consultants to develop the required documentation and record keeping system required by FDA, the company is now well prepared for future FDA applications."

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Bioenvision Inc. (Amex: BIV) of New York said it has filed an investigational New Drug Application to evaluate the efficacy of Modrenal (trilostane) for androgen-independent prostate cancer.

Modrenal is approved in the U.K. for advanced post-menopausal breast cancer, and was commercially launched in 2003, the company said.

The phase II open label clinical trial in prostate cancer would enroll 43 patients, staged in two groups over 12 months, the company said. Once a single positive response is seen in the first group of 18 patients, a further 25 will be enrolled. The primary endpoint of the study will be the prostate-specific antigen response. The criteria for response are defined according to the recommendations of the PSA working group and require a greater than 50 percent decrease in PSA from baseline on two measurements at least four weeks apart, the company said.

"We are intrigued with recent data suggesting Modrenal acts through modulating the beta isoform of the estrogen receptor, a target of great interest in prostate cancer research," said Principal Investigator Matthew Smith, assistant professor of medicine, Harvard Medical School, Massachusetts General Hospital. "Given this novel putative mechanism of action, coupled with clinical data showing the drug is active in advanced breast cancer, we are very interested in studying its effects on prostate cancer."

Modrenal, which acts as an ER beta modulator, increases estrogen binding to ER beta and decrease binding to ER alpha, the company said.

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CuraGen Corp. (Nasdaq: CRGN) of New Haven, Conn., said FDA has granted orphan drug designation to CG53135 for radiation induced oral mucositis.

The drug, which is in phase I trials, is an investigational protein. It promotes epithelial and mesenchymal cell proliferation in vitro and is active in animal models of OM, the company said.

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NeoPharm Inc. (Nasdaq: NEOL) of Lake Forest, Ill., said it has reached an agreement with FDA under the special protocol assessment on its

phase III randomized evaluation of convection enhanced delivery of IL13-PE38QQR with survival endpoint, for first recurrence of glioblastoma multiforme.

The SPA process allows for a written agreement between NeoPharm and FDA on the design of a study, including clinical drug supply, pivotal trial design, clinical endpoints, study conduct, data analysis, and other clinical trial issues, and is intended to provide assurance that if pre-specified trial results are achieved, they may serve as the primary basis for an efficacy claim in support of a biologics licensing application, the company said.

The trial was designed to compare overall survival, drug safety and quality of life of patients receiving IL13-PE38QQR with patients receiving Gliadel Wafer for GBM following surgical tumor resection, the company said. The trial would enroll 300 patients in multiple centers across North America, Europe and Israel. Patients will be randomized so that 200 patients receive IL13-PE38QQR via convection enhanced delivery using catheters placed following the resection, and 100 patients receive Gliadel Wafer placed at the time of resection, the company said.

The drug has received orphan drug designation in the U.S. and Europe, and Fast-Track drug development program status from FDA, the company said. NeoPharm has exclusively licensed IL13-PE38QQR from NCI and FDA, and is developing the agent under a CRADA in collaboration with the laboratory of Raj Puri, at the FDA Center for Biologics Evaluation and Research, the company said.

IL13-PE38QQR is a recombinant protein consisting of a single molecule composed of two parts: a tumor-targeting molecule (IL13) and a cytotoxic agent (Pseudomonas exotoxin, or PE), the company said. The data show that the cancer cell appears to latch onto and absorb the IL13, as well as the attached PE, which results in the death of the cancer cell.

* * *

Pfizer Inc. of New York, said it has received approval from FDA to market Fragmin (dalteparin sodium injection), a low molecular weight heparin, for prophylaxis of deep vein thrombosis or pulmonary embolism in acutely ill patients whose mobility is severely restricted.

Fragmin is a clot-preventing agent in the class known as low-molecular weight heparins, the company said.

Data from the Prostective Evaluation of Dalteparin Efficacy in Immobilized Patients Trial of 3,681 patients, show that hospitalized patients with cancer, congestive heart failure or respiratory failure who receive Fragmin 5000 IU once daily for 14 days had a 45 percent reduction by day 21 for developing clinically relevant DVT/PE compared to placebo, the company said. The benefit was maintained for the entire 90-day study period. Treatment with the agent resulted in low incidence of bleeding and thrombocytopenia.

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R2 Technology of Gaithersburg, Md., said the FDA Radiological Devices Panel of the Medical Devices Advisory Committee unanimously recommended approval of the ImageCheckerCT CAD system for the detection of lung nodules during review of multi-detector CT chest exams with conditions.

"Computer-aided detection provides a double read or additional notification to the radiologist of suspicious nodules that might go otherwise unnoticed," said Pablo Delgado, clinical associate professor of radiology at University of Missouri, Kansas City. "We are looking forward to being able to detect all nodules, including nodules caused by lung cancer."

The technology provides detection of nodules in chest CT exams taken for any clinical indication, not just for lung cancer screening studies, the company said.

Oncology Management:

Referral Guidelines Published For Care of Pelvic Masses

(Continued from page 1)

university-based, academic institutions.

The findings show that the guidelines can function as an effective tool to help direct the highest risk group of women with pelvic masses to specialty care, said the groups. In addition, a family history of ovarian and breast cancer in first degree relatives is less useful than the other four criteria-postmenopausal state, abnormal pre-operative CA-125 level, presence of ascites and evidence of abdominal or distant metastasis by exam and imaging study-in predicting ovarian cancer.

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M. D. Anderson Cancer Center said it has retained **Dumanli International** to facilitate information access and treatment referrals for Turkish patients seeking therapy at the Houston

cancer center.

Dumanli International, a health care consulting firm in Istanbul, works on behalf of U. S.-based health-related organizations and consults with patients seeking medical treatment abroad, the center said. The firm will assist with medical records management and travel arrangements, and provide administrative assistance to patients upon their return to Turkey.

"Through this new representation, we will offer Turkish patients with cancer their very best option for hope and survival," said Wendeline Jongenburger, director, International Program at M.D. Anderson. "We are excited about exchanging information with Turkish clinicians and sharing knowledge of the highest quality, research-driven patient care available."

* * *

Texas Cancer Care, of Fort Worth, Tex., said it plans to build the Center for Cancer and Blood Disorders in Fort Worth.

"Our vision has been to create the next generation in the delivery of cancer care, which is an inclusive center that will ensure integrated access to all components of the continuum of care," said William Jordan, president of TCC.

The center will be ready by early 2005, the company said. The center will provide medical oncology, radiation oncology; clinical research; a women's center; full radiographic and laboratory diagnostic capabilities; a resource library; a community multi-purpose center; a chapel and meditation area; a complementary medicine center, including oncology specific massage; and a nutrition and psychosocial center.

Clinical Trials:

Celsion To Amend Phase I Trial Of ThermoDox For Prostate Ca

Celsion Corp. (AMEX:CLN) of Columbia, Md., said FDA has allowed two amendments to its phase I dose escalation study of ThermoDox, a liposome-encapsulated formulation of doxorubicin, for prostate cancer.

The original phase I protocol was limited to cancer that had spread beyond the prostate, the company said. Based upon safety data for the first two groups of patients, FDA has allowed expansion patients with progressive prostate cancer in-situ. In addition, the company was permitted to add an additional site, Grand Strand Urology in Myrtle Beach, SC, to its existing clinical sites at Roswell Park Cancer Institute and New York and Regional Urology in Shreveport, Louisiana, the company said.

The therapeutic approach combines focused-heat thermotherapy with the heat-activated drug ThermoDox, a formulation in which doxorubicin is encapsulated in a heat-activated liposome, the company said. The prostate is heated to 41 degrees C with the Celsion Microfocus BPH 800 Microwave Urethroplasty system, which enables the systemically administered ThermoDox to release its encapsulated doxorubicin, the company said.

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Hudson Health Sciences Inc. of South San Francisco said it has begun enrollment in a phase I trial of PT-523 for solid tumors.

The multi-center, open label, dose escalation trial will investigate the safety, tolerability, pharmacokinetics (including maximum tolerated dose) and preliminary efficacy of the compound for advanced solid tumors where curative or survival prolonging therapy has failed or where no therapies exist, the company said.

PT-523 is a multi-targeted antifolate anti-cancer drug that is a water-soluble, non-polyglutamatable, type-B analogue of aminopterin, the company said. It was developed at the Dana-Farber Cancer Institute and at NCI as part of a program to develop therapies with improved efficacy, tolerability and resistance.

"PT-523 has the potential to be an important new treatment for oncology," said Joseph Eder, clinical director, Experimental Therapeutics at Dana-Farber Cancer Institute, assistant professor of medicine at Harvard Medical School and lead investigator. "The research into this novel compound could provide significant benefit to patients with very limited and inefficient treatment options."

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OSI Pharmaceuticals Inc. (NASDAQ:OSIP) of Melville, N.Y., said it has expanded a phase I trial of OSI-461 for advanced solid tumors.

The study has been amended to see whether administering OSI-461 with food may increase drug exposure levels achievable following oral dosing of OSI-461, the company said.

OSI-461 is a second-generation molecule in a class of drugs known as selective apoptotic anti-neoplastic drugs, and is part of the SAANDs technology platform which OSI acquired from Cell Pathways Inc. in 2003.

"Although we have seen some initial hints of

anti-tumor activity in pilot phase II studies in prostate, chronic lymphocytic leukemia and renal carcinoma, we do not believe we have yet optimized dose with this agent," said Nicole Onetto, executive vice president and chief medical officer at OSI Pharmaceuticals. "We have observed a positive effect of food on drug exposure in pre-clinical models and we would anticipate moving into more robust proof-of-concept studies with OSI-461, if we can reproduce this in humans."

OSI-461 also is being evaluated in a series of preliminary phase II studies in chronic lymphocytic leukemia, renal cell carcinoma and prostate cancer, the company said. In the prostate cancer study, one patient had a minor response and one patient had an unconfirmed reduction of greater than 50 percent in PSA levels out of 29 patients who received 200mg or 400mg BID of OSI-461. No serious drug-related adverse events were seen in the study. The OSI-461 program also includes a phase II study moderate to severe Crohn's disease.

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Schering-Plough Research Institute of Kenilworth, N.J., said it has stopped enrollment in its phase III trial of Sarasar (lonafarnib) in non-small-cell lung cancer.

An analysis of interim data from this study led to the conclusion that the study will not provide sufficient evidence of efficacy to warrant further enrollment, the company said.

SPRI said it is continuing its phase II clinical studies of Sarasar in leukemia and a variety of solid tumors. Schering-Plough noted that other companies' anticancer compounds trastuzumab and gefitinib also have failed to show efficacy in their recent studies in first-line NSCLC.

Sarasar is designed to inhibit farnesyl transferase, an enzyme involved in the regulation of the growth and proliferation of cancer cells, the company said.

* * *

SpectRx Inc. (OTCBB: SPRX) of Norcross, Ga., said it is initiating clinical trials of its non-invasive cervical test by submitting final protocols to hospitals participating in the multi-site study.

Development of the non-invasive cervical cancer test is supported by a $1.4 million grant from NCI, $767,000 of which will go toward completing the trial this year, the company said. A completed NCI-supported pre-pivotal clinical study indicated that the test could reduce by 55 percent the number of unnecessary follow-up procedures as a result of false positive Pap test results.

The device uses proprietary technology to identify cancers and precancers painlessly and non-invasively by analyzing light reflected from the cervix, the company said. The device creates an image of the cervix that highlights the location and severity of disease. The technology distinguishes between normal and diseased tissue by detecting biochemical and morphological changes at the cellular level. Unlike Pap or HPV tests, the non-invasive test does not require a tissue sample or laboratory analysis, and results are available immediately, the company said.

Deals & Collaborations:

Alteris Licenses Vaccine From Duke And Hopkins

Alteris Therapeutics Inc. of Philadelphia said it has licensed additional rights to its lead therapeutic vaccine, ALT-110, from **Duke University** and **Johns Hopkins University**.

ALT-110 is a therapeutic vaccine targeting EGFRvIII , a tumor-specific splice variant of the epidermal growth factor receptor, the company said.

Both universities have taken an equity stake in Alteris as part of the licensing agreement, the company said. ALT-110 was originally identified by Albert Wong, founder of Alteris, while at Johns Hopkins.

Alteris has previously licensed other technology rights relevant to ALT-110 from Thomas Jefferson University, the company said.

Splice variants result when sections of a gene are shuffled to create alternative forms of proteins, the company said. The proteins can include growth factors, which are associated with major diseases like cancer. EGFRvlll, a splice variant discovered by Wong in brain tumors, is also found in more than 70 percent of breast and ovarian cancers and 100 percent of metastatic prostate cancers, the company said.

The treatment is in a phase I trial at the University of Washington School of Medicine through collaboration with the SouthWestern Oncology Group, the company said. The trial is partly supported by the Rapid Access Investigational Drug program of NCI.

EGFRvIII stimulates the growth of cancer as a result of its ability to enhance tumor cell survival, proliferation, invasion and growth of new tumor blood vessels, the company said. ALT-110 is a peptide designed to recruit immune system defenses to target

the receptor to stop or slow the growth of cancer cells. Because EGFRvIII has only rarely been observed in normal human tissues, it is a target for cancer therapy, the company said.

In a mouse model of tumors containing EGFRvIII, administration of ALT-110 either prevented tumor growth or induced existing tumors to regress, the company said. Preclinical studies also demonstrated that ALT-110 generates two different types of immune response—an antibody and a cellular response—to tumor cells containing the EGFRvlll receptor.

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National Institute of Biomedical Imaging and Bioengineering at NIH and the **Center for Devices and Radiological Health** at FDA said they signed an interagency agreement establishing a joint Laboratory for the Assessment of Medical Imaging Systems to assess and optimize high-resolution, high-dimensional medical imaging systems.

Co-directors of the program are Peter Kirchner, acting director of the Intramural Science Program, NIBIB, and David Brown, director of the Division of Electronics and Computer Science, Office of Science and Technology, CDRH.

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Apax Partners Funds of London said **Medeus Pharma Ltd**., a company created by Apax Partners with Bryan Morton, CEO of Medeus Pharma, said it is closing on its acquisition of the **Elan Corp.** European sales and marketing business for $120 million.

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ChemBridge Research Labs. LLC of San Diego and **ChemBridge Corp**. said **CRL**, **ChemBridge**, and **Pfizer Inc.** have amended their strategic alliance agreement and have entered into another discovery chemistry collaborative agreement, which would extend until 2008.

The expansion is based on the performance shown by both CRL and ChemBridge during the first two years of their alliance with Pfizer, the companies said. The arrangement also expands the scale and the scope of the alliance to include hit-follow- up and medicinal chemistry support for the Pfizer Global Research and Development organization.

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CMS of St. Louis has entered into a strategic partnership with **iKnowMed** to merge in 2004.

"The collaboration will provide more complete patient history and treatment information to clinicians across the multi-disciplinary cancer team," said Don Simborg, president, CEO, and founder of iKnowMed. "The synergy of our two companies links the information flow between the treatment paths of chemotherapy and radiation therapy."

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Jerini AG of Berlin and **Merck KGaA** of Darmstadt said they have entered into a collaboration agreement to develop small molecule inhibitors against an undisclosed target for oncology.

Under the agreement, Jerini will receive an upfront payment, personnel funding, milestone payments, and royalties, the companies said. Merck obtains worldwide rights for all indications in cancer, cardiovascular diseases, diabetes, and thyroid disorders.

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Merck & Co. Inc. of Whitehouse Station, N.J., and **Aton Pharma Inc**. of Tarrytown, N.Y., said they have entered into a definitive agreement under which Merck will acquire Aton.

Under the agreement, Merck will acquire 100 percent of the equity of Aton and Aton will become a wholly owned subsidiary of Merck.

The Aton lead product candidate, suberoylanilide hydroxamic acid, is in in phase II trials for cutaneous T-cell lymphoma, the companies said.

"The other co-founders and I are delighted with the Merck transaction" said Paul Marks, co-founder of Aton Pharma and president emeritus of Sloan-Kettering Cancer Center. "Merck gives us the best opportunity to see our drugs for the treatment of cancer reach the marketplace. That has always been our most important goal."

* * *

Seattle Genetics Inc. (Nasdaq:SGEN) of Bothell, Wash., entered into an agreement with **Abbott Laboratories** (NYSE:ABT) to manufacture the SG SGN-30 monoclonal antibody.

The antibody is also used in the SG SGN-35 antibody-drug conjugate.

Under the agreement, Abbott would perform scale-up and GMP manufacturing for clinical trials, as well as supply commercial-grade material to support potential regulatory approval and commercial launch, the company said.

SGN-30 is a genetically engineered monoclonal antibody that targets CD30-positive hematologic malignancies, the company said. SG said it is conducting phase II trials of the product for Hodgkin's disease and anaplastic large cell lymphoma.

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