THE CANCER LETTER INTERACTIVE

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Bristol Stock Drops Amid New Setbacks, Deepening Firm's Decline In Oncology

For decades, Bristol-Myers Squibb Co. was the dominant player in oncology and cancer politics.

Bristol operatives were on first-name basis with leading academics. Professional societies and advocacy groups turned to the company for money. The NCI drug discovery pipeline seemed to connect directly with Bristol's development program, and the Institute's cooperative groups could count on the company for access to experimental drugs.

As Bristol ruled, generics shuddered at the thought of encounters with the company's black-suit-clad ninja squad of "franchise extension"

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In Brief:

Elias Zerhouni Nominated For NIH Director; Richard Carmona For Surgeon General

PRESIDENT BUSH made two nominations to fill top federal health posts last week. Bush nominated **Elias Zerhouni** for NIH director and **Richard Carmona** for Surgeon General.

Zerhouni is executive vice dean of the Johns Hopkins University School of Medicine, chairman of the Department of Radiology and Radiological Science, and a professor of radiology and biomedical engineering. Zerhouni also has served on the NCI Board of Scientific Advisors.

"Leading the NIH is a great responsibility, and I have picked the right man to do so," Bush said in his March 26 announcement. "Dr. Zerhouni and his wife [Nadia Zerhouni] immigrated to America from Algeria with $300 in their pocket, but a dream of opportunity…. He is an expert in biomedical research, and is committed to extending his benefits to all Americans, and all humanity.

"Dr. Zerhouni will also bring strong management skills to the NIH, and they are needed," Bush said. "This is a large and complex organization. The NIH budget has grown dramatically from around $2 billion in 1975 to more than $23 billion today. And my 2003 budget proposes an additional increase of nearly $4 billion. I urge Congress to approve this increase, and when they do, we will have completed my campaign commitment to double funding to this vital medical research over the next five years.

"Dr. Zerhouni is well-prepared to manage this rapidly growing institution during times of great new opportunity and urgent biodefense needs," Bush said. "He has supervised research at Johns Hopkins, one of

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Bristol CEO Ousts Head Of Pharmaceutical Unit

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specialists.

Now, the company's hegemony in oncology is threatened, or, more likely, lost forever. Earlier this week, Bristol's Chairman and CEO Peter Dolan admitted to Wall Street that the company's projected drug sales were "off-track" and the company's performance "unacceptable."

"We clearly must improve," Dolan said to analysts in a telephone conference April 3.

The setbacks Dolan listed included:

—U.S. wholesalers have excessive inventories of Bristol products. "The company has begun to reduce shipments in an attempt to lower inventories to levels more consistent with market demand," Dolan said. The value of excessive inventory is estimated at $800 million to $1 billion.

—Because of decreasing sales of several products, first-quarter sales would be likely to decline by about 7 percent from the first quarter of 2001. As a result, the company has lowered projected earnings by 25 to 30 percent, to $0.44 to $0.47 per share. For the full year, too, sales are expected to decline by 25 to 30 percent.

On April 4, the day after the announcement, Bristol stock dropped by 14.7 percent to $32.15 per share, roughly half of its value a year ago, when Dolan took over the top job at the company.

The announcements come at a time when generics are starting to market lower-priced versions of Bristol's core drugs, Taxol, Glucophage, and BuSpar. In other setbacks, last December, FDA refused to consider the application for C225, a compound Bristol licensed from ImClone Systems Inc, and last month, a study found that Bristol's cardiology drug Vanlev was marginally more effective and probably more toxic than the Merck drug Vasotec, which is available in generic form.

"The company's current business performance is unacceptable and I am taking steps today, and may take additional actions in the future, as necessary, to strengthen our organizational structure, focus our priorities and accelerate our future growth," Dolan said in a statement. "I recognize that today's announcement may have a negative impact on our results in the short term, but it is absolutely necessary that we take concrete steps today in order to position Bristol-Myers Squibb for the long term. We have a proud history as a leader in the pharmaceutical industry, and I will take necessary steps to assure that we maintain and build upon this heritage."

Dolan announced a corporate shake-up, ousting Richard Lane, head of the worldwide pharmaceutical unit, and promoting Donald Hayden from his current post as executive vice president of the health-care group to executive vice president of the company and president of the North American medicines division.

Hayden is a former director of the Bristol oncology division and one of the survivors of the company's glory days. Though he is respected in oncology, Hayden will be faced with having to shore up an organization that has lost many of its valuable employees.

Problems in Bristol's oncology franchise began to emerge in the mid-1990s, as the company appeared to have lost focus on the field, insiders and outside observers concur. Oncology was merged with immunology, and became a part of a sprawling pharmaceutical empire.

Though Bristol has looked at many drug candidates to fill its pipeline, it has not secured an FDA approval of an oncology drug since Dec. 28, 1992, when the agency gave a green light to Taxol. In fact, the last two Bristol oncologists who had shepherded a drug through approval are no longer in the oncology division. One of the two, Marcel Rosenzweig, has retired, and the other, Renzo Canetta, has been moved to franchise extension.

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Over the past year, a large number of Bristol oncology specialists have either found better jobs, were fired, or retired. The list of alumni includes: Rick Winningham, senior vice president for oncology and immunology; Tim Whitten, senior vice president for global oncology marketing; Thomas Jordan, vice president of global oncology marketing; Kathleen Deardorff, vice president for marketing; Beth Seidenberg, senior vice president for global development at the BMS Pharmaceutical Research Institute; Jeff Humphrey, director of clinical research; Garnett Dezember, a former oncology official who became vice president for global marketing in infectious diseases; and Hemanshu Shah, director of marketing. Also gone is Joel Lasker, general counsel at the BMS pharmaceutical group. Lasker's retirement was announced last year, in the midst of an event known to Bristol insiders as the "Valentine's Day Massacre." Several members of Lasker's staff were discharged that day.

With this much turmoil, it is unclear whether Dolan will be able to remain in his job and whether Bristol will manage to remain independent, observers say.

The prospect of a takeover may shore up the price of Bristol's stock. "We are maintaining our long-term Strong Buy rating as we believe that the company's stock price will be buoyed by the speculation that it could be an acquisition target," wrote Merrill Lynch First Vice President Steven Tighe.

Bristol officials declined to comment.

NCI Programs:

Advisors OK New Program For Bone Metastasis Grants

Advisors to NCI unanimously approved the Institute's plan to set aside $12.3 million over the next five years to fund grants for research on molecular interactions between tumor cells and bone.

NCI currently funds about $5.4 million of research in the area of bone metastasis, while the total grant support in tumor metastasis is approximately $48 million, Division of Cancer Biology program director Suresh Mohla said to the Board of Scientific Advisors at its March 25 meeting.

The success rate for R01 grants in bone metastasis was 20 percent in FY 2001, compared to a 30 percent success rate for other R01s, Mohla said.

Congressional reports on the NCI FY 2002 budget encouraged the Institute to "develop a better understanding of the unique role the bone microenvironment plays in metastasis of cancer to the bone, in particular breast cancer, prostate cancer, and myeloma."

Recent developments suggest that bone metastasis offers great scientific opportunity, according to the concept statement Mohla presented to the board. These include: the availability of a number of experimental models to study bone metastasis in prostate and breast cancer, and multiple myeloma; implantation of human bone in SCID mice, allowing successful homing of prostate cancer and multiple myeloma cells to human bone; availability of high-throughput technologies and laser capture microdissection to permit evaluation of complex interactions; and significant advances in basic bone biology research has enabled the formation of a large cohort of basic biologists who could enter the field of bone metastasis.

Excerpts from the text of the concept statement follow:

Molecular Interactions Between Tumor Cells and Bone. Concept for a new RFA, first-year set-aside $3 million, to fund six R21s and 6 R01s, two to five years. Total estimated cost for project period $12.3 million. Program director: Suresh Mohla, Division of Cancer Biology, Tumor Biology & Metastasis Branch, tel: 301-435-1878, email: sm82e@nih.gov.

This initiative encourages independent and established investigators to submit applications to promote a better understanding of the pathophysiology of bone metastasis especially as it relates to tumor cell-bone interactions, and delineation of the mechanisms involved in tumor metastasis to the bone. NCI strongly believes in the need to invest in expanding the knowledge in this area, through utilization of new technology as well as encouragement of collaborative teams of investigators, which would greatly contribute to understanding molecular events that account for homing of tumor cells to the bone. Research that is directed toward elucidating the fundamental biology will provide the leads for new treatment strategies, and diagnostic and prognostic tools. The funding mechanisms proposed will be traditional and exploratory grants (R01s and R21).

The overall objective is to have a better understanding of the unique features of the bone and its microenvironment that renders it an attractive site for tumor cells. Areas in which such scientific opportunities exist include, but are not limited to:

Tumor cell-bone interactions: The identification of the molecular interactions between tumor and bone cells has previously used the candidate gene approach, but is ready for the judicious application of gene array technology to identify new targets. Tumor growth does

not appear to be a major point of regulation of bone metastasis, although growth is the most common parameter assayed in vitro. Microarray identification thus needs to use RNA from metastatic versus non-metastatic cells and be coupled to an efficient system for validating physiological significance of identified candidate genes in animal models. Alternative approaches which address these issues should also be considered.

The relationship between tumor cell adhesion to bone marrow endothelial cells and its subsequent acquisition of motility, migration, and invasive phenotype need to be elucidated. The mechanism by which the turnover of bone, bone matrix proteins and wound healing affect the process of cancer cell dissemination to bone is an area that needs examination. The key transcription factors that are turned on and are required to maintain cancer cell survival in visceral and bone sites need to be identified.

One of the interesting aspects of the bone microenvironment-tumor interaction is the difference between mouse and human. The issue of why human tumor cells prefer to colonize human bone, but not mouse bone, is yet to be addressed.

Factors that promote bone metastases: There are several mechanisms that contribute to bone metastasis, namely i) Synthesis, activation, and presentation of extracellular matrix-degrading proteases thought to be critical in enabling metastatic breast cancer cells to cross multiple barriers and spread to distant tissue. Studies to identify and determine the functional signature of proteolytic mechanisms, however, are in their early stages; ii) The molecules associated with preferential adhesion of invading tumor cells to the bone endothelium; iii) Bone-associated cytokines which act as chemoattractants; iv) Cytokines, survival factors and anti-apoptotic signals that support the growth and survival of cancer cells in the skeleton. These are areas that need to be actively pursued.

Critical signaling pathways: The nature of the signaling pathways whereby hormones, growth factors, and adhesion molecules modulate metastasis to the bone is poorly understood. For example, nm23, HER-2/neu, and p53 are several non-protease genes associated with metastases, but despite intense study, the exact mechanism for their association with increased metastatic potential remains obscure. A comprehensive analysis of genetic changes occurring between primary tumor and bone metastases and the development of a tractable system to study bone metastases are needed.

Specific roles of osteoblasts, osteocytes, and osteoclasts: Most research, until now, has focused on osteolytic metastases and suggests that osteolytic factors (such as PTHrP and IL-11) stimulate osteoclasts indirectly by activating the RANK ligand pathway on osteoblastic cells. A role for the osteocyte in metastasis remains unaddressed and needs to be studied.

Tumor cell-endothelial cell interactions: The role of angiogenesis in bone metastasis remains largely unexplored. It has been demonstrated that endothelial cells of various organs carry specific cell-surface addresses, which can be modulated by cytokines as well as the stromal and extracellular matrix environment with which they interact. A comparison of gene expression profiles of endothelium derived from normal and tumor tissue revealed a number of genes specifically elevated in tumor-associated endothelium. Many of these tumor endothelial cell markers were expressed in a wide range of tumor types as well as in normal vessels associated with wound healing, corpus luteum formation. Although specific molecular adhesive interactions between circulating tumor cells and bone marrow endothelia have been shown in vitro, their physiological importance in vivo remains to be tested. The mechanisms by which tumor cells interact with bone endothelial cells and the role of the extracellular matrix in these interactions need to be delineated. Identification of critical factors involved in tumor cell survival and colonization in the bone environment need to be identified and their mechanisms delineated.

Role of the immune system: The bone marrow is the primary site of hematopoiesis in the adult. To fulfill this role, the stroma and the cytokine environment of the bone marrow are specialized to support the growth of lymphocytes and other hematopoietic cells. These elements have a variety of direct and indirect effects on bone growth. For example, many immune modulators (IFN, IL-1, -6, -18 and others) have potent effects on osteoclast formation, and RANK ligand is a T cell product. Osteoprotegrin not only neutralizes RANKL, but also TRAIL, which stimulate immune cell destruction of breast cancer cells. Very little is known about how such factors relate to other elements of the bone microenvironment, indicating that the role of immune cells in tumor bone interactions has been understudied.

Systemic host effects: Standard treatment of cancer patients with chemotherapy creates a state of high bone turnover secondary to suppression of sex steroids. High bone turnover may well enhance metastases to bone. This important question can be studied with available animal models. For a number of candidate factors involved in bone metastases, such as endothelin-1, VEGF, and PDGF, effective small molecule inhibitors are already available, such as receptor antagonists for endothelin and receptor kinase inhibitors of VEGF and PDGF. The roles of these molecules in bone turnover are less well understood and the effects of the inhibitors need to be tested in preclinical animal models of normal bone homeostasis.

Advisors Plan Reorganization Of Oncology Study Sections

Advisors to the NIH Center for Scientific Review have developed a plan for restructuring the study sections that review grant applications in oncology.

The ONC Study Section Boundaries Team, a working group of scientific leaders in oncological research, recommended the proposed new structure at a meeting in December 2001. The plan is part of the CSR's overall restructure of its study sections.

"This proposal represents a significant change in the structure of study sections that review applications in this area," according to a CSR statement.

The proposed structure of the Oncological Sciences Integrated Review Group, which would include 13 study sections, was released recently and is available for public comment until June 10.

According to the proposal, the Oncological Sciences IRG will consider "applications involving basic, translational, and clinical investigations that encompass cancer prevention, initiation, promotion, progression, and treatment. Specifically, the ONC IRG reviews research grant applications related to chemical carcinogenesis, cancer genetics, nutritional carcinogenesis, radiation effects, and tumor biology; mechanism of action of cancer therapeutic agents in both *in vitro* and *in vivo* model systems; development and evaluation of experimental therapies of neoplastic diseases, translation of basic research to clinical practice; development or optimization of treatment modalities; chemoprevention; and development of biomarkers/signatures for tumor detection and diagnosis."

The IRG will include the following 13 study sections:

Cancer Etiology Study Section (CE)

Cancer Genetics Study Section (CG)

Cancer Immunotherapy Study Section (CI)

Chemo/Dietary Prevention Study Section (CDP)

Drug Discovery and Molecular Pharmacology Study Section (DMP)

Developmental Therapeutics Study Section (DT)

Clinical Oncology Study Section (CONC)

Diagnostic Oncology Study Section (DOSS)

Radiation Therapeutics and Biology Study Section (RTB)

Tumor Cell Biology Study Section 1 (TCB-1)

Tumor Cell Biology Study Section 2 (TCB-2)

Tumor Microenvironment Study Section (TME)

Tumor Progression and Metastasis Study Section (TPM)

The new guidelines can be found at http://www.csr.nih.gov/PSBR/ONC/ONC.pdf. A roster of the working group that developed the guidelines is available at http://www.csr.nih.gov/PSBR/ONC/ONCRoster.pdf. Comments on the plan may be made at http://www.csr.nih.gov/PSBR/ONC/ONCIntro.htm.

After the comment period ends, NIH will review the comments, obtain additional information as necessary, and recommend appropriate modifications. A report on the new proposed IRG and study section guidelines will be presented to the CSR Advisory Committee. The committee will review the final draft guidelines and make recommendations to the CSR director.

Youth Smoking, Up In 1990s, Begins To Decline, NCI Says

Adolescent smoking rates increased through much of the 1990s, but a new report released this week by NCI shows there has been a decline over the past few years.

The report provides the first major update of adolescent smoking behavior since 1994. It concludes that there is a need for more research and anti-smoking programs designed to prevent young people from starting to smoke and to help them quit. The report reveals a particular need for research among certain racial/ethnic groups where smoking trends have not decreased or, in some cases, continued to increase.

"Changing Adolescent Smoking Prevalence: Where It Is and Why" was compiled by over 30 U.S. public health experts. David Burns, of the University of California, San Diego, was the senior scientific editor of the monograph.

Smoking initiation rates for males at all ages have declined in recent years, but there was little evidence of a decline in initiation for females under 16 years old. Initiation rates increased for females 16 years and older.

The youth smoking rates overall remain relatively high. The latest figures reported in the monograph are from the 2000 Monitoring the Future study, which showed that almost 32 percent of 12th-graders are current smokers (defined as having smoked within the past 30 days).

The highest rate of current smoking for 12th-graders in the 1990s occurred in 1997, with almost 37 percent reported as current smokers.

According to "Healthy People 2010," the government's comprehensive set of health objectives for the nation, the goal is to reduce the percent of current adolescent smokers to 16 percent by the year 2010.

"Much work and continued progress are needed in order to reach that goal," said Scott Leischow, chief of NCI's Tobacco Control Research Branch.

Several chapters in the NCI monograph present data on various racial/ethnic groups, including descriptions and explanations of smoking behavior among African American, Hispanic/Latino, Asian American and Pacific Islander, and American Indian and Alaskan Native adolescents. Smoking rates vary by ethnic group, with American Indian and Alaskan Native adolescents showing the highest rate and African American adolescents showing the lowest.

The authors describe protective factors—such as religious involvement and participation in high school sports programs—that may contribute to lower smoking rates in certain populations, and risk factors—such as poverty—that might lead to higher smoking rates in others.

The monograph addresses large-scale influences on the smoking behavior of adolescents, including access, marketing, and cost of tobacco products. The data on youth access show that young people continue to obtain cigarettes both from noncommercial sources, such as friends and family members, and from commercial sources, such as convenience stores, even though cigarette sales are prohibited to individuals under the age of 18.

The data on the effect of cost show that youth are more responsive to cigarette price increases than are adults. A 10 percent increase in the price of cigarettes is estimated to reduce youth smoking by 5 percent or more. In addition, evidence exists that youth are more likely to quit smoking as cigarette prices are increased.

Chapters in the monograph also explore the results from statewide tobacco control programs in Massachusetts, California, and Florida. The authors examine the predictors of tobacco use among youth and describe the impact of the programs. In California, for example, following the enactment of Proposition 99—which provided tobacco control groups with funding to launch an aggressive anti-smoking campaign—adolescent smoking showed a significant decrease compared with the national rates, particularly among adolescent males.

"The evidence indicates that sustained programs work when they address the full range of influences on youth tobacco use, such as tobacco-free policies, active parent and community involvement, school-based programs, cessation services, and media to counter tobacco advertising," Leischow said. "But the monograph reminds us that there is no easy solution for reducing youth smoking. Tobacco control organizations and researchers must continue to find answers and implement comprehensive policies and programs that are proven effective."

The monograph is available at http://cancercontrol.cancer.gov/tcrb/nci_monographs. To order a copy, see NCI's Publications Locator Web site at http://www.cancer.gov/publications or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237).

Funding Opportunities:
Program Announcements

PAR-02-074: Innovative Toxicology Models for Drug Evaluation: Exploratory/Developmental Grants and Phased Innovation Award

Letter of Intent Receipt Dates: July 26, 2002; March 26, 2003; Nov. 25, 2003

Application Receipt Dates: Aug. 23, 2002; April 23, 2003; Dec. 23 2003

NCI encourages the development, standardization, and validation of new and innovative assays which determine or predict specific organ toxicities (e.g., hematotoxicity, cardiotoxicity, gastrointestinal toxicity, hepatotoxicity, nephrotoxicity, ototoxicity, bladder toxicity, neurotoxicity, pulmonary toxicity, and endocrine toxicity, including pancreatic beta cell toxicity) as well as new methodology for high throughput toxicity screening which involves the use of molecular endpoints, computer modeling, proteomics and genomics. Genetically modified animals or cell lines, various non-mammalian organisms, in vitro assays utilizing primary mammalian cells (human cells are of particular interest), tissue slices, isolated organs, sub-cellular fractions or purified enzymes could be utilized for the model. Computer modeling utilizing existing biological and toxicological data bases would be appropriate. Genomic and proteomic technology. The PA will use the NIH R21, R33, and the combined R21/R33 phased-innovation award mechanisms. The PA is available at http://grants1.nih.gov/grants/guide/pa-files/PAR-02-074.html.

Inquiries: Adaline Smith, NCI, Division of Cancer Treatment and Diagnosis, Toxicology and Pharmacology Branch, 6130 Executive Blvd, Rm 8036, MSC 7451, Bethesda, MD 20892-7458, Rockville, MD 20852 (for courier service), phone 301-496-8777; fax 301-480-4836; e-mail smithad@mail.nih.gov

NOT-AI-02-010: Inter-Institute Pilot Program for the Development of AIDS-Related Therapeutics

Letter of Intent: May 1, 2002

Application Receipt Date: June 1, 2002

The program, which is designed to help AIDS research investigators facilitate the preclinical development of: 1) therapies for the treatment of HIV disease, AIDS-associated malignancies, opportunistic infections and tuberculosis associated with AIDS, and 2) microbicide-based prevention strategies for HIV, is co-sponsored by the National Institute of Allergy and Infectious Diseases and NCI. IIP does not fund grants. Instead, applications are requests to use IIP drug development resources to conduct specific tasks the applicants themselves are unable to carry out in their efforts to translate basic research findings to applied or clinical practice. Examples of tasks that may be requested include High Throughput Screen assay development, evaluation in animal efficacy models, Good Manufacturing Practice scale-up synthesis of small molecules and biologics, clinical dosage formulation and manufacturing, and Good Laboratory Practice toxicology. The notice is available at http://grants1.nih.gov/grants/guide/notice-files/NOT-AI-02-010.html.

Inquiries: IIP coordinator, 6130 Executive Blvd., Suite 8000, Rockville, MD 20852, phone 301-496-8720; e-mail iip@dtpax2.ncifcrf.gov

RFP Available

RFP: Evaluation of Chemopreventive Agents by In Vivo Screening Assays

NCI's Division of Cancer Prevention, Chemoprevention Agent Development Research Group, is interested in evaluating inhibitors or potential inhibitors of any stage of carcinogenesis to identify chemopreventive agents against cancer. Such agents are to be further evaluated in appropriate toxicological or clinical settings. The CADRG has established a clearly defined integrated plan for evaluation of chemopreventive agents, which delineates detailed criteria for classifying the quantity and quality of information that currently exists on any chemopreventive agents and thus defines what additional information and investigations are required to qualify the agent's experimental use in intervention trials of human cancer. The primary purpose of the RFP is to evaluate chemopreventive agents In Vivo for inhibition of carcinogenesis to establish the relative efficacies of selected chemopreventive agents in at least one animal model system. The North American Industry Classification System code is 54171.

Inquiries: For information and an electronic copy of the RFP, contact Dorothy Coleman (by e-mail), contracting officer, Prevention, Control Population Sciences Section, Research Contracts Branch, NCI, Bethesda, MD 20892-7195, phone 301-435-3829; fax: 301-402-8579; e-mail dc93a@nih.gov .

Foundation Offers Grants In Cancer Survivorship

The Lance Armstrong Foundation seeks to promote the optimal physical, psychological, and social recovery and care of cancer survivors and their loved ones.

For 2002, the foundation will emphasize a disciplined study of cancer survivorship through peer-reviewed grants. The foundation is particularly interested in applications on the following topics: Physical Activity and Survivorship, Adolescent/Young Adult specific projects, and applications that would ultimately yield validated interventional programs. Proposals must be hypothesis-driven and be able to collect, validate, and analyze information to answer questions. Ongoing survivorship programs will not be considered.

Deadline for receipt of final submissions is July 15, 2002. It is anticipated that successful applications will be announced in December 2002 with funding beginning Jan. 1, 2003. The yearly budget of the proposed grant may not exceed $50,000 and can be renewable for up to three years, pending annual review and approval of work in progress by the foundation. Indirect costs may be included but cannot exceed 10%. Budgets should initiate Jan. 1, 2003. Overlapping funding from other sources will not be allowed.

Further information: Lance Armstrong Foundation, Priya Sircar, 2901 Bee Caves Road, Box L, Austin, TX 78746, tel: 512-236-8820, fax: 512-236-8482, email: grants@laf.org.

RFA Available

RFA CA-03-006: Chemoprevention of Tobacco-Related Cancer in former Smokers: Clinical Studies

Letter of Intent Receipt Date: June 21, 2002

Application Receipt Date: July 26, 2002

The initiative funds clinical research pilot clinical trials (phase I/II or phase II) evaluating the efficacy of chemopreventive agents in specified cohorts of former smokers with or without a prior history of a tobacco-related malignancy and translational studies performed on specimens (such as tissue, blood, urine, etc.) derived from these clinical trials. NCI intends to commit approximately $4,000,000 in FY 2003 to fund 3 to 5 new and/or competitive supplement grants to existing cooperative agreements in response to the RFA. An applicant may request a project period of up to 5 years and a budget for direct costs of up to $1,000,000 per year.

The RFA is available at http://grants1.nih.gov/grants/guide/rfa-files/RFA-CA-03-006.html.

Inquiries: Eva Szabo, Division of Cancer Prevention, NCI, 6130 Executive Blvd., Rm 2132, MSC 7341, Bethesda, MD 20892, phone 301-435-1595; fax 301-480-3924; e-mail szaboe@mail.nih.gov.

In Brief:

Carmona, Zerhouni Named To Top Federal Health Posts

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our nation's leading research facilities. One former colleague calls him a quadruple threat: a doctor who excels at teaching, researching, patient care and management. Dr. Zerhouni shares my view that human life is precious, and should not be exploited or destroyed for the benefits of others. And he shares my view that the promise of ethically conducted medical research is limitless. As Director of the NIH, Dr. Zerhouni will be at the forefront of our efforts to promote biomedical research with a careful regard for the bounds of medical ethics."

Carmona is a clinical professor of surgery and clinical assistant professor of family and community medicine at the University of Arizona. He is also the chairman of the state of Arizona Southern Regional Emergency Medical System. He served in Vietnam as an Army Green Beret as a police officer in Pima County, Arizona.

Carmona "will bring to the Surgeon General's Office a proven commitment to service, and a strong management background," Bush said. He outlined three priorities for the next Surgeon General: emergency preparedness for the threat of bioterrorism; improving Americans' diet and exercise habits; and reduction of drug and alcohol abuse.

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CENTERS FOR DISEASE CONTROL and Prevention will be led by a management team until a director is appointed, HHS said. **David Fleming**, deputy director for science and public health, was named acting director. The management team will include **James Hughes,** director of the National Center for Infectious Diseases, and **Julie Gerberding,** acting deputy director of NCID, will head bioterrorism efforts. **Michael Osterholm**, director of the Center for Infectious Disease Research and Policy at the University of Minnesota, will serve as a representative to Secretary Tommy Thompson during the transition, until a permanent director is appointed. **Jeffrey Koplan**, current CDC director, plans to retire on March 31. . . . **NCI SEARCH COMMITTEE** has been formed to recommend a new director for the Division of Cancer Treatment and Diagnosis. DCTD Director **Robert Wittes** left last month to take the post of physician-in-chief, Memorial Sloan-Kettering Cancer Center. Deputy Director **Alan Rabson** serves as chairman of the search committee. Wittes held the title of DCTD director as well as Deputy Director for Extramural Science, overseeing the cancer centers, SPOREs, and training programs, the Office of Cancer Complementary and Alternative Medicine, the Office of Clinical Research Promotion, and the Office of Informatics. NCI Director **Andrew von Eschenbach** told the NCI Board of Scientific Advisors that he will study the organizational structure before filling the extramural science position. . . . **R01 PAYLINE** for fiscal 2003 would increase from the 21st percentile to the 23rd or 24th percentile under the Bush Administration's proposed budget for NCI of $4.7 billion, von Eschenbach told the board.

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Appointments: **JOSEPH BERTINO**, program chairman of molecular pharmacology and therapeutics at Memorial Sloan-Kettering Institute for Cancer Research, was appointed professor of medicine and pharmacology at the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School and associate director at the Cancer Institute of NJ. He was also designated a UMDNJ University Professor. . . . **RICHARD BARAKAT**, surgeon and clinical investigator, has been appointed chief of the Gynecology Service at Memorial Sloan-Kettering Cancer Center. . . . **H. LEE MOFFITT CANCER CENTER** made the following appointments: **Clay Smith** has been named chief of the Blood and Marrow Transplant Service and program leader of BMT and the Department of Interdisciplinary Oncology. **Karen Fields**, chief of medicine service and medical director of affiliations, has been named interim associate DIO chair for clinical affairs and the interim DIO program leader for the Comprehensive Breast Program. **David Tatro**, assistant vice president of human resources at Inova Health System in Virginia, has been appointed vice president of human resources at Moffitt.

* * *

Awards: **JUNE DAHL**, University of Wisconsin Comprehensive Cancer Center, executive director of the American Alliance of Cancer Pain Initiatives and co-founder of the Wisconsin Cancer Pain Initiative, received the Distinguished Service Award from the American Pain Society. . . . **DEBRA GORDON**, University of Wisconsin Hospital and Clinics, former board member of the American Alliance of Cancer Pain Initiatives, member of the Wisconsin Cancer Pain Initiative, received the Clinical Practice Award from the American Society of Pain Management Nurses.

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