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FDA Says ImClone Data Insufficient To Evaluate Colorectal Cancer Drug C225

FDA last week declined to review the application by ImClone Systems Inc. for C225, a treatment for colorectal cancer patients who develop progressive disease following treatment with CPT-11.

The agency's "refusal to file" letter for C225 said the data presented by the company were insufficient to evaluate the Biologics License Application for the therapy.

ImClone (Nasdaq: IMCL) planned to present its application for
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In Brief:

Congress Approves \$4.19 Billion For NCI, \$23.5 Billion For NIH, In FY2002 Appropriation

NCI's **FIRST \$4-BILLION BUDGET:** NCI is slated to receive a \$4.19 billion appropriation for fiscal 2002, a 12 percent or \$450 million increase over last year's budget, under the Labor-HHS-Education spending bill that came out of conference committee Dec. 19 and passed by Congress. As of this writing, the bill has not been signed by President Bush, but all indications are that it will be. "We're absolutely delighted with the proposed 2002 budget," NCI Acting Director **Alan Rabson** said to **The Cancer Letter**. "It will give us enough money to continue to support the many programs that (former NCI Director) Dr. **Richard Klausner** started." The President's request for NCI early this year was \$4.17 billion, and the NCI Bypass Budget for FY2002 sought \$5.03 billion. The bill provides \$23.5 billion for NIH, a \$3 billion increase that continues on the trajectory of doubling the NIH budget over the past five years. Congress also approved a bioterrorism spending measure within the Department of Defense for \$71 million to increase security at NIH and the Centers for Disease Control and Prevention, and \$55.8 million for bioterrorism and disaster response in the office of the HHS Secretary. . . . **RICHARD KLAUSNER**, former NCI director, was appointed senior fellow and special advisor for counterterrorism at the National Academies, just 10 weeks after leaving NCI to direct a new research institute. On Sept. 11, Klausner announced his departure from NCI to become founding president of the Case Institute of Science, Health and Technology, to have been funded initially for \$100 million by AOL Time Warner Chairman **Steve Case** and his wife **Jean Case**. "At this critical juncture, all that science and technology can offer must be channeled into finding ways to protect Americans from the threats of terrorism," Klausner said last month. "Having the unique opportunity
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FDA Letter Cites Problems With ImClone's C225 Studies

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accelerated approval of C225 to the Oncologic Drugs Advisory Committee in February. The drug's trade name is Erbitux and the generic name is cetuximab.

Last fall, Bristol-Myers Squibb Co. bought a 20-percent stake in the New York-based biotechnology firm for \$1 billion, and co-licensed C225 in a transaction that could add up to another \$1 billion if C225 is approved. ImClone's regulatory approval strategy was in place before the transaction with Bristol, and under the deal, ImClone is responsible for the filings.

The FDA letter was dated Friday, Dec. 28, and was announced after the stock market closed. In a telephone conference for the press and the financial community before the reopening of the market on the morning of Dec. 31, ImClone officials assured Wall Street that the agent had met clinical endpoints, and that the FDA concerns involved documentation that could be reproduced.

"We feel that this is not a drug that failed to meet its clinical endpoints," Samuel Waksal, the company president and CEO, said at the conference. "However, the company did fail to provide a proper train of documentation which would allow the agency to accept this filing."

According to Waksal, the agency was unable to

assess the patients' eligibility and their subsequent performance in the pivotal trial. In that trial, patients refractory to CPT-11 were treated with CPT-11 and C225.

A copy of the agency's refusal-to-file letter obtained by **The Cancer Letter** indicates that the problems with the trials were more extensive than the absence of the "train of documentation" and involved the structure of the trials. According to the nine-page letter:

—The company's pivotal trial was not "adequate and well controlled."

—The trial was not designed to demonstrate the contribution of CPT-11 to the regimen.

—New clinical trials would be needed to provide more robust data documenting response and to compare the efficacy of the single agent C225 to the combination of C225 and CPT-11.

—The application does not justify the proposed dosage of C225, and additional pharmacokinetic information is needed.

—The pivotal trial contains protocol violations.

—Reporting of deaths within 30 days of last treatment with C225 is incomplete. The agency identified 21 patients who died within a month of the last treatment with C225, but the company provided narratives for only three of those patients.

"The exchange between the agency and us is right now a confidential exchange, because we are working with the agency to try and put together a response that allows us to move forward with our BLA," Samuel Waksal said to **The Cancer Letter**. "We didn't release the letter, so whatever you have, you have from an illegitimate source."

Waksal said the refusal-to-file letter lays the groundwork for the company's discussions with FDA. "The letter that we got from FDA raises issues," he said. "It doesn't raise corrective measures. We are going to meet with the agency, give them the corrective measures we are going to use, find out if it's good enough, and then we will let you know what they say."

Regulatory issues notwithstanding, C225 works, Waksal said.

"This is an approvability issue; not an acceptance issue," Waksal said in an interview. "And the approvability issue will be publicly aired at ODAC, and if ODAC feels that we don't have enough data to warrant approvability of this drug, that's one thing. I don't think that they will think that. I don't think that anyone believes that this drug doesn't have dramatic



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activity.”

The agency’s decision to refuse the ImClone submission is likely to have important implications in oncology, observers said. First, the potential of failure of C225 could impede Bristol’s chances of acquiring a blockbuster drug it needs to replace Taxol, a drug now available from generics.

The FDA action could also mean some tightening of what so far has been a generous mechanism of accelerated approval, based on “surrogate endpoints” that may translate into benefits to patients. Accelerated approval is usually based on nonrandomized phase II trials.

C225 is a monoclonal antibody that targets the Epidermal Growth Factor Receptor expressed on the surface of some cancer cells.

Samuel Waksal “Stunned”

According to the FDA document, ImClone was repeatedly informed about the problems with its clinical trials. However, at the company telephone conference, Samuel Waksal said he was unaware of the problems with the application

“I was rather stunned when we got the letter,” Waksal said at the conference. “I have to tell you, this was unexpected. I didn’t have plans to end the year this way.”

In an interview, Waksal said he was stunned in part because such letters from FDA are uncommon. “A lot of these questions could have been answered during the review process,” Waksal said to **The Cancer Letter**. “Refusal-to-file letters don’t come that often, and we believe that a lot of the pieces that were missing would not be something that would constitute a refusal to file.”

At the conference Dec. 31, Waksal offered something of a mea culpa for his company’s failure to anticipate that FDA would require data for assessing each patient’s eligibility and performance.

“Obviously, some mistakes may have been made,” Waksal said at the conference. “We had believed, obviously, that in-between documentation was not the gating factor. Obviously, that’s not the case.” Waksal said the company had the data, and would be able to provide the documentation the agency required.

When the market opened on Dec. 31, the price of the company’s stock dropped by 19 percent.

The issue of verifying eligibility is fundamental in clinical trials. “The company said that FDA was not challenging the response rate, but it may have

been that FDA could not even address that issue until they got better documentation, so that’s why the application wasn’t allowed in the door,” said Mace Rothenberg, associate professor of cancer research at Vanderbilt Ingram Cancer Center, a gastrointestinal cancer expert who was not involved in development of C225.

“The big issue here is whether they can go back and go through the documentation they have, and include the requested information in the revised BLA that will then meet the satisfaction of FDA to allow filing, or whether that documentation never was obtained in the first place,” Rothenberg said.

At the conference, company officials said the data were available for demonstrating the patients’ eligibility and performance, and the process would be completed in the next few months.

Originally, ImClone was responsible for regulatory filings, while Bristol stood on the sidelines. This hands-off arrangement has changed, ImClone officials said. The biotech company is now working with BMS to respond to the agency’s questions.

“BMS is clearly playing an increased role,” ImClone executive vice president Harlan Waksal said to **The Cancer Letter**. “We have gone to them to ask for their help and expertise.”

At the conference, Samuel Waksal described the interaction between the two companies as “seamless.” “It will be as if its one group [is] moving forward to rectify all the issues,” he said.

Many of the questions raised by FDA involve the operation of the Independent Radiology Advisory Committee, IRAC, assembled by ImClone to review patient data from the pivotal trial.

The committee included two radiologists and two oncologists who read the scans to determine the patients’ eligibility and their response to treatment. The committee members worked independently from each other, and whenever disagreements arose, they had to come to a consensus in assessing each case.

ImClone officials said at the conference that the committee’s determinations were in concordance with the determinations of investigators who treated the patients at the trial’s 40 sites.

“The concordance of the response rates is very solid, both between the institutions where the studies were run and with the IRAC,” Harlan Waksal said at the conference. “However, most important is to provide the data in a clear way, so when reviewers take a look at this information, they can follow the train of thought, and without any question reach the



same conclusion. Obviously, we did not prepare this documentation well enough for them to do so. That train of thought—the ability to take the cases and move through each one—wasn't clear enough for the agency to accept this filing.”

Will the Studies be Repeated?

To be eligible for the company's pivotal trial, patients had to fail a regimen containing CPT-11. After treatment failure was documented, these patients were treated with a combination of CPT-11 and C225.

According to a paper presented at last year's annual meeting of the American Society of Clinical Oncology, 22.5 percent of the 120 patients treated achieved an objective response to the two-drug regimen.

Though the trial was designed to assess potential synergy between the two compounds, in an earlier meeting with the company, FDA officials said that the trial design makes it impossible to separate the activity of CPT-11 from the activity of C225.

As a result, the company initiated a smaller, confirmatory trial of C225 as a single agent, company officials said. That trial enrolled 57 patients and produced an objective response in 6 patients, an 11-percent response rate, the FDA letter said. Patients enrolled in the confirmatory trial were taken off CPT-11 regimens, and the trial did not make use of IRAC.

Company data cited by FDA reports that the pivotal trial of the two-agent regimen had the 95% confidence interval of 15.4%, 30.5%. The single-agent trial had the 95% confidence interval of 4%, 21.5%.

At the Dec. 31 conference, ImClone officials acknowledged the possibility that studies may have to be repeated.

“If we cannot provide the evidence in such a way that makes the agency accept the package, then the clinical trial is not going to be sufficient for approval,” Samuel Waksal said. “However, that is not what we believe is going to happen. Hopefully, we won't need to prove anything else, because we believe that we have the data available—the data exists in its raw form.”

The FDA letter states that new studies would be needed.

To begin with, the application does not contain data that isolates the contribution of CPT-11 to the combination regimen, the letter states.

According to the agency, the company was told repeatedly that data demonstrating the contribution of each of the agents would be required.

“In order for your application to be considered complete, you were informed during the meeting of Aug. 11, 2000, in our letter of Jan. 19, 2001, and during the telephone conference call of Jan. 26, 2001, that the application must provide evidence that the addition of a toxic agent (irinotecan [CPT-11]) is necessary to achieve the clinical effect,” the letter states.

“The data do not show that the response rate observed with the combination of cetuximab [C225] and irinotecan could not also be observed with single agent cetuximab at the dose and schedule proposed.”

The pivotal trial was not “adequate and well controlled,” the letter states. “Because we... have determined that the current study was not adequate and well controlled... and that robustness of the overall response rate is less than is stated in the study reports, you will need to conduct additional studies to provide this evidence.”

The agency suggested a “randomized, controlled trial directly comparing the efficacy of single agent cetuximab to the combination cetuximab plus irinotecan in patients who can be documented to be refractory to irinotecan therapy,” the letter said. “Alternatively, irinotecan therapy could be included as a third arm in a study enrolling patients who are not refractory to irinotecan.”

Deviations from the protocol are a problem, too, the letter states. This problem is not limited to the question of eligibility.

According to the agency, one patient was declared refractory and enrolled in the trial without a CT scan to evaluate response to CPT-11. No baseline scan was performed, and subsequent scans showed no evidence of metastatic disease.

The patient ultimately withdrew for reasons unknown, the letter states. Another patient received radiation three weeks before enrollment. Still another patient was treated with a nonstandard dose of CPT-11 before enrollment.

Justification for C225 Dosage Needed

“The application does not contain the data requested to support the proposed dose and schedule for cetuximab,” the FDA letter states. The agency said the issue of dosage is not new.

“During the Jan. 7, 1999, meeting, you indicated that saturation of tumor occurs at doses between 200 to 400 mg/m², and that a high dose is necessary because the liver and skin, along with the tumor, serve as ‘a sink’ for the elimination of the drug,” the letter



states.

The agency said it didn't concur with this analysis and asked repeatedly for justification of the dose.

"To correct this deficiency, you need to provide an integrated dataset and analysis of the pharmacokinetic profile of cetuximab," the letter states. "The analysis should support your statements regarding the relationship of the proposed dose and dosing regimen to clinical safety and effectiveness, the intensity of tumor EGFR expression and tumor burden in patients, and to in vitro and in vivo levels of cetuximab obtained in subjects receiving the proposed dose and schedule."

"The safety database is not complete and contains inconsistencies and discrepancies that preclude an accurate assessment of the toxicity profile," the letter states.

According to the document, FDA identified 21 patients who died within 30 days of the last treatment with C225. The company provided explanations for three of the deaths. "Narrative summaries are required for all patients who died during or within 30 days of administration of study drug or prior to resolution of treatment related toxicity," the agency states.

The letter was signed by Karen Weiss, director of the FDA Division of Clinical Trial Design and Analysis and Kathryn Stein, director of the Division of Monoclonal Antibodies. Both divisions are part of the FDA Center for Biologics Evaluation and Research.

Now What?

It will be a challenge for ImClone and Bristol to respond to the agency's concerns by organizing raw data into a format acceptable to FDA, experts say.

"I think FDA is going to want sequential CT scans that show that the tumor was progressing prior to study enrollment despite treatment with CPT-11, and another set of sequential scans demonstrating that a subset of patients responded for a clinically meaningful period of time as a result of treatment with CPT-11 and C225," said Rothenberg.

It is unclear whether the company would be able to use the same IRAC.

"We don't want to call the IRAC back in until we ask the agency what we need to say to IRAC," Samuel Waksal said at the conference call. "Remember, this IRAC has already reviewed these films. They already have seen them. They already have their bias. It may be that we need to redo all this."

After acquiring a stake in ImClone and licensing

the drug, Bristol paid the biotech company \$200 million. Had FDA accepted the application, the company would have received another \$300 million. Marketing approval would bring in \$500 million. Bristol stands to receive about 40% of the profits on C225 over the life of the product.

Bristol bought its stake in ImClone for \$70 per share, a considerable premium. Last September, when the deal was announced, ImClone shares were trading at about \$60. A month later, when the deal was completed, the price of shares dropped to about \$50.

All company stockholders had the opportunity to sell their stock at that time. According to company disclosures, shareholders who cashed in a portion of the stock last Oct. 29 included Samuel Waksal, who sold 815,000 shares, Harlan Waksal, who sold 775,000 shares, chairman of the board Robert Goldhammer, who sold 362,000 shares, and board member John Mendelsohn, who sold 90,000 shares. Mendelsohn, president of M.D. Anderson Cancer Center, pioneered the preclinical development of C225.

The C225 application was being processed under the FDA Fast Track mechanism.

ImClone is about to start a phase III study comparing the Saltz regimen of CPT-11, 5-fluorouracil and leucovorin with Saltz regimen plus C225 for the front-line treatment of advanced colorectal cancer, Samuel Waksal said to **The Cancer Letter**. A pilot study for the trial involving 30 patients was recently completed, and the company is starting to accrue patients for the 1,000-patient study, Waksal said.

Also, the company is conducting phase II trials of C225 in pancreatic cancer, head and neck cancer and non-small cell lung cancer, and phase III trials in combination with chemotherapy and radiation therapy as first-line treatment for head and neck cancer.

On Dec. 28, the day ImClone received the refusal-to-file letter, Astra-Zeneca filed a New Drug Application for Iressa, a small-molecule agent that is a potential competitor to C225.

Letter to the Editor:

Toxicity Of Saltz Regimen Should Remain A Concern

To the Editor,

We believe the article entitled "Safety Concerns About Saltz Regimen Were Statistical Artifact, ODAC Finds" (**The Cancer Letter**, Dec. 14, 2001) sent the wrong message. The fatal toxicity that is experienced



by a small proportion of patients receiving this regimen should remain a concern of all oncologists who treat patients with colorectal cancer.

In an ongoing trial, the North Central Cancer Treatment Group noted that 4.8% of patients with advanced colorectal cancer who were treated with the Saltz Regimen died within 60 days of starting treatment. This compares to a rate of 1.8% on the other two chemotherapy regimens in the same prospectively randomized cooperative group protocol (N9741) sponsored by the National Cancer Institute. Subsequently in the setting of postoperative adjuvant chemotherapy in stage III patients, the Cancer and Leukemia Group B independently reported a 2.2% rate of death within the first 60 days on the Saltz regimen, compared to 0.8% in patients treated with 5-FU/Leucovorin alone. These findings were published in the *New England Journal of Medicine*¹ and confirmed by an independent review that was published in the *Journal of Clinical Oncology*.² The independent, consistent findings of these two studies convince us that this is no statistical artifact. ODAC only discussed advanced colorectal cancer in its deliberations, and therefore the findings in the adjuvant setting were not considered.

The rapid discovery and subsequent action based on these events was made possible by a newly developed real-time toxicity monitoring system³. We continue to feel that rapid access to toxicity information is vital to the conduct of clinical trials, and helps ensure the safety of patients entering onto these trials. In addition, we feel that the use of an objective, easily interpretable measure of early toxicity, such as the number of deaths within 60 days of trial entry, is an important monitoring metric that will improve the quality and interpretability of clinical trial toxicity reporting. Members of the ODAC commended NCCTG and the cooperative groups on this process at their December 6 meeting.

At the ODAC meeting, Pharmacia presented a retrospective review spanning several decades of early mortality rates for a number of regimens used for the treatment of advanced colorectal cancer. Indeed other regimens such as the "Mayo Clinic" and "Roswell Park" regimens of 5FU and leucovorin appear to be associated with early mortality rates similar to that of the Saltz regimen. ODAC, in its deliberations, accurately concluded that it may not be Irinotecan (Camptosar) specifically that accounts for these early deaths. All of these regimens need to be given with caution, close monitoring, and early supportive

intervention to minimize risks to patients. The fact that 5-7% of patients on trials for the treatment of advanced colorectal cancer with a variety of regimens die within 60 days of study entry is a sobering fact. This illustrates that we sorely need to develop more effective and less toxic chemotherapy for this disease. In addition, efforts to develop tests allowing the prospective identification of patients susceptible to potentially lethal side effects are needed.

We agree with ODAC that the FDA package insert for Camptosar should continue to include the Saltz regimen for the palliative treatment of patients with advanced colorectal cancer. This regimen has demonstrated a two-month improvement in median survival in this setting.⁴ We feel that the label should provide more explicit warnings describing the potential for life threatening early toxicity, and guidelines for their management. At this time, there is no justification for use of the Saltz regimen in those patients who have undergone potentially curative surgery for their colon cancer.

Richard Goldberg
Michael O'Connell
Daniel Sargent
Mayo Clinic
Rochester, Minn.

(1) Sargent DJ, Niedzwiecki D, O'Connell MJ, Schilsky RL. Recommendation for caution with irinotecan, fluorouracil, and leucovorin for colorectal cancer. *N Engl J Med* 2001 Jul 12;345(2):144-5.

(2) Rothenberg ML, Meropol NJ, Poplin EA, Van Cutsem E, Wadler S. Mortality associated with irinotecan plus bolus fluorouracil/leucovorin: summary findings of an independent panel. *J Clin Oncol.* 2001 Sep 15;19(18):3801-7.

(3) Sargent DJ, Goldberg RM, Mahoney MR, Hillman DW, McKeough T, Hamilton SF, Darcy JM, Anderson VL, Krook JE, O'Connell MJ. Rapid reporting and review of an increased incidence of a known adverse event. *J Natl Cancer Inst.* 2000 Jun 21;92(12):1011-3.

(4) Saltz LB, Cox JV, Blanke C, Rosen LS, Fehrenbacher L, Moore MJ, Maroun JA, Ackland SP, Locker PK, Pirodda N, Elfring GL, Miller LL. Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. Irinotecan Study Group. *N Engl J Med.* 2000 Sep 28;343(13):905-14.

Funding Opportunities: **Minority Investigator Award**

Application Deadline: Feb. 15, 2002

National Surgical Adjuvant Breast and Bowel Project Foundation Inc. is accepting applications from investigators from a racial or ethnic minority group. The \$50,000 annual award, subject to yearly renewal, focuses on research designed to: 1) improve the care of patients with breast or colorectal cancer, 2) prevent breast or colorectal cancer, or 3) increase the enrollment of



patients from racial and ethnic minority groups to breast or colorectal cancer clinical trials. NSABP is committed to increasing the participation of all women and men in clinical research studies by supporting an increase in minority medical professionals. The start date for the award is May 15, 2000. An application may be obtained from the NSABP's Web site at <http://www.nsabp.pitt.edu>.

RFAs Available

RFA-RR-02-003: Centers for Biomedical Research Excellence

Letter of Intent Receipt Date: Jan. 18, 2002

Application Receipt Date: Feb. 25, 2002

The NIH National Center for Research Resources invites applications for Centers of Biomedical Research Excellence from investigators at independent biomedical research institutions or biomedical research institutions that award doctoral degrees in the health sciences or sciences related to health within IDeA eligible states. Collaboration with other non-doctoral degree granting and research performing institutes or institutions is encouraged. The application must have a thematic science focus in one research area, such as neuroscience, cancer, structural biology, immunology, or bioengineering, and may use basic, clinical or both research approaches to attain the goals of the proposed center. The scientific leadership provided by one or more established biomedical research faculty is critical to the success of this initiative, especially for the mentoring of promising junior investigators. The center is intended to support investigators from several complementary disciplines. It will enable the institution to develop a critical mass of investigators and enhance their competitiveness in a specific research area that accelerates the rate at which those investigators compete for other complementary NIH research grant support. The RFA will use the exploratory grant award mechanism P20.

Inquiries: W. Fred Taylor, Division of Research Infrastructure, National Center for Research Resources, NIH, 6705 Rockledge Dr., Bethesda, MD 20892-7965, phone 301-435-0760; fax 301-480-3770; e-mail taylorf@ncrr.nih.gov

Specialized Program of Research Excellence in Pancreatic Cancer

The initiative seeks to establish a SPORE in Pancreatic Cancer. The goals are to: 1) build capacity for interdisciplinary translational research in pancreatic cancer; 2) establish consortia to ensure appropriate access to pancreatic cancer patients and tumor tissues and promote the development of pancreatic cancer family registries; 3) expand the research base in pancreatic cancer via development and improvement of animal and in vitro model systems that can be translated into human disease applications; 4) promote collaborations between basic and clinical or applied research scientists; 5)

provide career development opportunities in translational pancreatic cancer research for both junior investigators and established scientists wishing to refocus their careers; and 6) develop extended collaborations in critical areas of research need with laboratory, clinical, and population scientists in the parent and other institutions.

Inquiries: Jorge Gomez, Organ Systems Branch, Office of Centers, Training and Resources, ODDES, NCI, phone 301-496-8528; e-mail jg1w@nih.gov

Program Announcements

PAR-02-037: Small Grants Program for Behavioral Research in Cancer Control

Application Receipt Dates: April 22, 2002, Aug. 20, Dec. 20, April 21, 2003, Aug. 20, and Dec. 22.

The NCI Division of Cancer Control and Population Sciences invites research applications in cancer control from new investigators or established scientists refocusing their research interests to behavioral research in cancer. The program encourages research in settings, such as hospitals, universities, cancer centers, communities, schools, health departments and worksites. Studies may contribute to the design, implementation or evaluation of intervention programs, descriptive baseline surveys, testing, modification and validation of surveys or program materials for use in the proposed population groups, testing of recruitment, intervention or compliance procedures for participants, etc. Support will be through individual research project grants R03.

Inquiries: Veronica Chollette, Division of Cancer Control and Population Sciences, NCI, 6130 Executive Blvd, Suite 4100, MSC 7331, Executive Plaza North, Rockville, MD 20892, phone 301-435-2837; e-mail vc24a@nih.gov

PAR-02-040: Developmental/Pilot Projects in Cancer Complementary and Alternative Medicine

Letter of Intent Dates: Jan. 16, 2002, May 17, Sep. 16, Jan. 16, 2003, May 23, Sept. 16.

Application Receipt Dates: Feb. 20, 2002, June 21, Oct. 21, Feb. 20, 2003, June 20, Oct. 21.

The NCI Office of Cancer Complementary and Alternative Medicine and the National Center for Complementary and Alternative Medicine invite research grant applications developmental pilot research investigating complementary and alternative medicine in cancer. The initiative encourages the development of basic and clinical CAM cancer research. The PA is available at <http://grants.nih.gov/grants/guide/pa-files/PAR-02-040.html>.

Inquiries: Wendy Smith, OCCAM, NCI, Executive Plaza North, 6130 Executive Blvd, Suite #102, MSC 7302, Bethesda, MD 20892-7302, phone 301-435-7980; fax 301-480-0075; smithwe@mail.nih.gov



In Brief:

Klausner To Serve As Advisor On Bioterrorism For NAS

(Continued from page 1)

as a citizen and a scientist to take on this critically important challenge led me to make the difficult decision to forgo my involvement in establishing the Case Institute." Klausner will serve as liaison between **John Marburger**, the director of the White House Office of Science and Technology Policy, and new counterterrorism efforts of the Academies. "Rick is an outstanding leader who has made many innovative contributions to science and technology policy," said **Bruce Alberts**, president of the National Academy of Sciences. "In this time of special need, the Academies are extremely fortunate to be able to harness his energies and abilities for a critical new role." The centerpiece of the Academies' counterterrorism work is the Committee on the Science and Technology Agenda for Countering Terrorism, which Klausner will continue to co-chair with physicist **Lewis Branscomb**. The committee will identify high-priority research agendas, focusing on biological, chemical, nuclear, and radiological threats; information technology; transportation; energy facilities, buildings, and fixed infrastructure; and behavioral, social, and institutional issues. Klausner plans to continue running his NCI lab. . . . **MICHAEL O'CONNELL** was named director the new clinical cancer center and chairman of medical oncology at Allegheny General Hospital in Pittsburgh. He will work with Norman Wolmark, chairman of human oncology at Allegheny General and the National Surgical Adjuvant Breast and Bowel Project. O'Connell plans to start his new job around April 1. O'Connell, who has worked at Mayo Clinic for the past 27 years, also plans to continue as chairman of the North Central Cancer Treatment Group through the group's reverse site visit and the Mayo Clinic Cancer Center site visit in 2003, and will travel to Rochester monthly. **Jan Buckner** will assume responsibility for the operational management of the NCCTG Research Base. "We plan to establish a new NCCTG Group Chair Office located in Pittsburgh during my tenure," O'Connell wrote in a letter to colleagues. "We envision possible new relationships between NCCTG and NSABP that can notably benefit both organizations." . . . **HAROLD VARMUS**, president of Memorial Sloan-Kettering Cancer Center, announced on Dec. 26 the appointments of **Robert Wittes** as physician-in-chief of Memorial Hospital,

and **Thomas Kelly** as chairman of the Sloan-Kettering Institute. Wittes, who trained at Memorial Hospital and served as an attending physician in its Department of Medicine for 10 years, is NCI Deputy Director for Extramural Science and director of the Division of Cancer Treatment and Diagnosis. Wittes announced his plans for leaving NCI last month (**The Cancer Letter**, Dec. 7, 2001). Kelly, a noted physician-scientist, has spent his career at Johns Hopkins University, where he directs the Department of Molecular Biology and Genetics and the interdisciplinary Institute for Basic Biomedical Sciences. "Memorial Sloan-Kettering is beginning a period of extraordinary growth and development across our full panoply of clinical and research programs," said Varmus. "In Bob and Tom, we have leaders with the vision, skill and experience to work with me to guide Memorial Sloan-Kettering at this exciting time." Varmus joined MSK two years ago after serving as NIH director. Wittes succeeds **David Golde**, who announced his intention to step down as physician-in-chief earlier this year. Kelly succeeds Richard Rifkind, who retired as chairman of the Sloan-Kettering Institute in 1999. . . . **SIDNEY KIMMEL CANCER CENTER** in San Diego received a \$12 million gift from the Sidney Kimmel Foundation to support the center's strategic plans, developed as part of the recruitment of new President and CEO **Albert Deisseroth**. Among the programs scheduled to benefit from the gift is the Icon Clinical Trial, which is expected to be administered next spring through the Sidney Kimmel Cancer Center/Sharp HealthCare Clinical Trials Network. The trial will test an experimental therapy for cancer treatment. The gift, which will be distributed in four installments, will support the expansion of faculty and research infrastructure at the Sidney Kimmel Cancer Center, including a third research building. . . . **CHRISTOPHER MCCABE**, Maryland state senator, was named head of the Health and Human Services Office of Intergovernmental Affairs on Dec. 31. He becomes the top advisor to Secretary **Tommy Thompson** and departmental liaison on state, local and tribal governments issues. McCabe was a senior associate and director of development for the Johns Hopkins Medical Institutions. . . . **MULTIPLE MYELOMA** Research Foundation 2001 Friends for Life Gala raised \$1.1 million for myeloma research. **Ann Curry**, Today Show anchor, accepted the MMRF Public Awareness Award for her segment on the foundation and public education on cancer.



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