THE CANCER LETTER

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Grassley, House Republicans Launch Investigations Of I-ELCAP Conflicts

By Paul Goldberg

The Republican members of the House Committee on Energy and Commerce have launched an investigation of conflicts of interest in the International Early Lung Cancer Action Program.

Separately, Sen. Chuck Grassley (R-Iowa) asked NIH to explain how the I-ELCAP leaders have been able to obtain federal research funding, which they commingled with money received from a tobacco company.

The probe by House Republicans, announced in a June 6 letter to the NIH Director Elias Zerhouni, creates an unusual case of dueling investigations within the same House committee.

The Grassley probe, announced in a June 4 letter to Zerhouni, considers

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I-ELCAP Controversy:

Journals Probe Whether Rush University Official Broke Publication Embargo In Pro-CT Editorial

By Paul Goldberg

Two journals are trying to ascertain how James Mulshine, the top medical research administrator at Rush University in Chicago, gained access to an unpublished paper, apparently breaking a journal's publication embargo.

In late April, Mulshine, a former NCI intramural scientist who serves as an associate provost for research at Rush University Medical School, vice president for research at Rush University Medical Center, and director of Rush Translational Sciences Consortium, published an editorial in support of computed tomography screening for lung cancer.

The paper, which appeared in The Oncologist, included an extensive discussion of an original research paper that was about to be published in the journal Radiology, stating that the paper was "in press." Such quotation of material is not uncommon, but is always done with consent of the authors.

In this case, the authors say they had not consented to the publication and had not given Mulshine copies of their paper.

"Anyone engaged in research needs to play by those rules, and has no right to publish other people's data without their permission," Bruce Chabner, editor in chief of The Oncologist and clinical director at the MGH Cancer Center, Massachusetts General Hospital, said to The Cancer Letter.

In an "expression of concern" which has been attached to the Mulshine

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House Republican Probe Counteracts Democrats' Action

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the I-ELCAP issue in the context of NIH oversight of conflicts on the part of extramural scientists.

"Over the past number of years, I have become increasingly concerned about the lack of oversight regarding conflicts of interest relating to the almost $24 billion in annual extramural funds that are distributed by the NIH," Grassley, the ranking member of the Senate Finance Committee, wrote in a letter that uses I-ELCAP as one of five examples of conflicts on the part of federally funded medical researchers.

As they focus on conflicts of interests on the part of the leaders of the movement for computed tomography screening for lung cancer, the two investigations are likely to continue to focus public attention on the controversy that surrounds I-ELCAP, a group whose single-arm study is purported to have shown a dramatic survival benefit for screening.

The Democratic majority of the House Committee on Energy and Commerce, working with pro-screening groups, last fall started an exploration of alleged conflicts of interest in the NCI-sponsored National Lung Screening Trial, a randomized study criticized by proponents of screening (The Cancer Letter, Oct. 26, 2007).

Now, the Republican investigation would balance—or possibly neutralize—the Democratic probe, which was instigated by the proponents of screening before the conflicts of interest involving I-ELCAP leaders had surfaced in the media. These leaders, Claudia Henschke and David Yankelevitz of Weill Cornell Medical College, accepted $3.6 million in research funding from a tobacco company and failed to disclose patent, royalty, and consulting arrangements with manufacturers of medical equipment.

The story of I-ELCAP receiving funds from the Liggett tobacco company was broken by this publication and The New York Times, and has been carried by many national news outlets.

"I am concerned that the funding source and royalties may have not been disclosed when the NIH decided to fund Dr. Henschke," Grassley wrote in his letter.

The House Republicans' letter raises the question of the need to audit the I-ELCAP data. This idea first surfaced in an editorial in the April issue of The Oncologist. "Because of the importance of the I-ELCAP study and the questions raised regarding its results and sources of funding, it would seem to be of highest priority to have an independent audit of the clinical outcomes of the study, and a full disclosure of all sources of support, direct or indirect," wrote Bruce Chabner, clinical director of the MGH Cancer Center of the Massachusetts General Hospital and the journal's editor in chief.

Unlike the NLST data, the I-ELCAP data have never been independently audited.

"Would the NCI be able to audit the data or be interested in auditing the data?" asks the letter signed by Rep. Joe Barton (R-Tex.), ranking member of Energy & Commerce, and John Shimkus (R-Ill.), ranking member of the Oversight & Investigations subcommittee.

No major medical society recommends routine use of CT to screen current and former smokers. NIH hasn't yet responded to the queries from the Democrats, sources say.

Grassley views the probe of conflicts in the extramural program as a continuation of the ethics scandals in the intramural program.

"Dr. Zerhouni, you faced similar scandals back in 2003 when it came to light that many NIH intramural researchers enjoyed lucrative arrangements with pharmaceutical companies," Grassley wrote. "It took you some time, but you eventually brought some transparency, reform and integrity back to NIH. As you told Congress during one hearing, 'I have reached the conclusion that drastic changes are needed as a result of an intensive review by NIH of our ethics program, which included internal fact-finding as well as an external

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"NIH oversight of the extramural program is lax and leaves people with nothing more than questions—$24 billion worth of questions, to be exact. I am interested in understanding how you will address this issue. American taxpayers deserve nothing less."

The text of the House letter follows:

The National Institutes of Health has played a vital role in improving the public health of the United States for more than a century. Given the enactment of the National Institutes of Health Reform Act of 2006, we expect that NIH research efforts will provide the foundation for future scientific and medical advancement

We note with concern that the National Cancer Institute has been recently caught in the middle of a dispute between clinical researchers over whether former smokers and others at high risk for lung cancer should be screened using computed tomography scans. The NCI is attempting to help resolve this dispute by investing $200 million in a huge clinical trial called the National Lung Screening Trial, the largest cancer screening test ever conducted, hopefully generating data in 2010 to evaluate such CT scans, Last fall the leader of an advocacy group that favors such CT imaging for lung-cancer screening, unhappy that the NIH has not yet endorsed CT imaging, accused two researchers involved with NLST of bias and conflicts of interest because these researchers agreed to testify for tobacco companies about how screening might do more harm than good, The Majority side of this Committee has decided to pursue these accusations.

Several months later, The Cancer Letter and The New York Times published articles exposing potential conflicts of interest on the other side of the debate. These articles reported that the two leading researchers (part of a project known as the International Early Lung Cancer Action Project) who claim unprecedented success with CT screening for lung cancer have a financial stake in CT scanning technology used in their studies. Although these I-ELCAP researchers applied for 27 patents and have accepted royalty income from one license, they did not properly disclose these financial interests in medical journal articles, according to the Cancer Letter and the New York Times. In addition, these publications reported that most of the funds supporting the I-ELCAP researcher project came from a tobacco company gift of $3.6 million made to a foundation headed by one of the researchers.

It is not our purpose to weigh in on one side or the other in this dispute. Rather, our interest is in protecting America's interest in getting the best scientific evaluation on early lung cancer screening. To that end, we believe that there is a public interest in safeguarding the American taxpayer's $200 million investment in the NCI's National Lung Screening Trial, and in ensuring the integrity of NIH research. In light of those concerns, we respectfully request that the NIH provide the following information by June 16, 2008:

1. A status report on the NCI National Lung Screening Trial. Please include an explanation of NCI's expectation about the kind of data generated in 2010, and what kind of key results the NCI would be examining to reach any conclusions about the value of early lung cancer screening. Please identify any factors that could cause a delay in data being generated in 2010. Please also explain how the NCI has handled conflict-of-interest issues with respect to the researchers involved in the NLST.

2. Has the NCI audited the I-ELCAP data? If not, would the NCI be able to audit the data or be interested in auditing the data?

3. With respect to the I-ELCAP researchers, please explain whether the researchers individually or through their institution were receiving partial NIH support, and if so, whether they were required to disclose their financial stake in the CT scanning technology (including information on patents and royalties). If they were not receiving any NIH funds or they were not required to disclose, please explain under what circumstances a researcher receiving NIH funds would be required to disclose patent and/or royalty information. In addition, please explain whether and how NIH policy and/or regulations over NIH-funded researchers who set up private foundations to receive donations that also support NIH-funded research projects. Finally, do NIH policy and/or regulations require disclosure to the human subjects of the researcher's financial interests in patents and/or royalties, or about private donations supporting the study? If so, please explain and detail what the nature of the disclosure involved. If not, why not?

Grassley Questions NIH Extramural Oversight

The excerpted text of Grassley's letter follows:

I am dismayed to have read of funding provided to several researchers from the Foundation for Lung Cancer Early Detection, Prevention & Treatment. Dr. Claudia Henschke and Dr. David Yankelevitz are two of the Foundation's board members. As reported by *The New York Times*, the Foundation was funded almost entirely with monies from tobacco companies, and this

funding was never fully disclosed.

Monies from the Foundation were then used to support a study that appeared in *The New England Journal of Medicine* back in 2006 regarding the use of computer tomography screening to detect lung cancer.

The NEJM disclosure states that the study was supported also by NIH grants held by Drs. Henschke and Yankelevitz.

Regarding the lack of transparency by Dr. Henschke and Dr. Yankelevitz, National Cancer Institute Director John Niederhuber told the *Cancer Letter*, "[W]e must always be transparent regarding any and all matters, real or perceived, which might call our scientific work into question."

The NEJM later published a clarification regarding its earlier article and a correction revealing that Dr. Henschke also received royalties for methods to assess tumors with imaging technology.

There is no evidence that the Foundation's tobacco money or Dr. Henschke's royalties influenced her research. But I am concerned that the funding source and royalties may have not been disclosed when the NIH decided to fund Dr. Henschke.

Grassley asks the following questions:

—Since reports appeared in the press regarding the undisclosed funding of the Foundation for Lung Cancer: Early Detection, Prevention & Treatment, what steps has/will NIH take to address this issue? Please provide all external and internal communications regarding this issue.

—Please provide a list off all NIH grants received by Dr. Claudia Henschke. For each grant, please provide the following:

a. Name of grant;

b. Topic of grant; and

c. Amount of funding for grant.

—Please provide a list of any other interactions that Dr. Henschke has had with the NIH to include membership on advisory boards, peer review on grants, or the like.

—Please provide a list off all NIH grants received by Dr. David Yankelevitz. For each grant, please provide the following:

a. Name of grant;

b. Topic of grant; and

c. Amount of funding for grant.

—Please provide a list of any other interactions that Dr. Yankelevitz has had with the NIH to include membership on advisory boards, peer review on grants, or the like.

I-ELCAP Controversy:

Authors Say Mulshine Cited Paper Without Permission

(Continued from page 1)

paper in The Oncologist, Chabner notes that the paper quoted research that was about to be published by the journal Radiology "without the knowledge or the permission of the authors of that primary paper."

"We have requested an explanation from Dr. Mulshine and concomitantly publish this Editorial Expression of Concern," Chabner wrote. "Further editorial action(s) may be taken, as warranted."

On the Rush website, Mulshine is described as "the primary academic officer responsible for all aspects of the research enterprise." According to his curriculum vitae, he is a member of the editorial boards of seven journals, including Clinical Cancer Research, International Journal of Oncology and Oncology, and has taken part in peer review for 16 journals, including the New England Journal of Medicine, the Journal of the National Cancer Institute, the Journal of Clinical Oncology, Blood, Cancer, Cancer Research and the European Journal of Cancer.

Mulshine didn't respond to calls and emails from The Cancer Letter.

Mulshine's editorial was accepted by The Oncologist on March 24 and published online on April 30. The paper he cited—"Estimating Long-term Effectiveness of Lung Cancer Screening in the Mayo CT Screening Study," by Pamela McMahon et al.—was published online by Radiology almost a week later, on May 5.

A spokesman for Radiology said Mulshine was neither a reviewer nor an editor on the Radiology paper.

"We are currently looking into the matter and will respond in more detail when we have further information," said Maureen Morley, assistant director of public information and media relations at the Radiological Society of North America, which publishes the journal. "It is not unheard of to cite an article that is in press. However, author permission must be obtained, which does not appear to have been done in this case."

The fact that the paper was discussed at length in The Oncologist didn't affect Radiology's publication schedule, Morley said. "The article in The Oncologist had no impact on when the McMahon study was published online [by Radiology]," she said.

Authors Say They Didn't Grant Permission

Discussion of the Radiology paper takes up nearly a quarter of Mulshine's editorial, presumably because its top-line result appears to part ways with other modeling papers and suggests a modest mortality benefit for CT screening for lung cancer.

G. Scott Gazelle, the senior author of the Radiology paper and professor of radiology and health policy at Harvard and director of the Massachusetts General Hospital's Institute of Technology Assessment, said he first learned about Mulshine's citation from a colleague, who called to ask for a copy of the paper.

"I said, 'No, sorry, it hasn't been published yet, and it's subject to an embargo," Gazelle recalled. "I will be happy to send it as soon as it's published."

Immediately after that conversation, Gazelle contacted Mulshine. "I sent him an email, saying I was interested to read your comments, but wanted to know where you got our manuscript, because it's not published," Gazelle said. "He responded that he got it from the Radiology website. I responded that I doubted that, since it wasn't published on the Radiology website."

Responding to Gazelle's request, Mulshine provided him the version of the paper he used in preparing the editorial, Gazelle said.

"If you were to see this, you would see something that is double-spaced, has line numbers on it, and is clearly not something that would have been obtained from the Radiology website," Gazelle said. "It's not a formatted Internet publication version. It's a manuscript draft. I would not cite it without contacting the authors and asking for permission or without confirming that it had been published."

Only two authors listed on that paper had electronic copies of the version that ended up in Mulshine's possession. They were Gazelle and the lead author McMahon, also of the MGH Institute for Technology Assessment.

Gazelle said the draft was prepared for consideration by the Cancer Information and Surveillance Network, a consortium of NCI-sponsored investigators who use modeling in assessment of cancer prevention, screening, and treatment.

"It was the version that only existed to be distributed through CISNET, a group of seven sites [of lung cancer researchers], who have a signed confidentiality agreement not to distribute it outside of the group," Gazelle said. "So, at least one person in CISNET violated that agreement and either directly sent it to Jim Mulshine or sent it to somebody else who sent it to Jim Mulshine." Mulshine is not a member of the consortium.

On March 24, the day the Mulshine paper was accepted by The Oncologist, the Radiology paper was far form being ready for publication. "We hadn't even sent back the galley proofs by then," Gazelle said. "There was no way that Radiology would have posted it on their website.

Mulshine's explanation appeared to have evolved, Gazelle said.

"His initial position was that he got it from the Radiology website, and therefore didn't think he needed to have permission," Gazelle said. "Once he came to the realization that he didn't get it from the Radiology website, he said, 'Well, you know, I am busy, it was my best-faith effort. I thought it was a legitimate version.'"

Though scientific papers often circulate informally before publication, the journals' embargoes are broken rarely, usually by bloggers or reporters, journal editors say.

When embargoes are broken, sanctions are rare. Journalists cannot be punished unless they had consented to an embargo a priori. Those who receive materials is advance of publication can get struck from the lists.

Medical researchers who disclose embargoed materials can be barred from publishing in the affected journals. However, corrections and expressions of concern represent a more ominous threat since they appear on searches of medical literature and affect the scientists' reputation and their ability to publish.

Last year, the New England Journal of Medicine reportedly imposed sanctions against a peer reviewer who publicly discussed the paper he had reviewed before it was published. The journal apparently barred the researcher, a cardiologist, from reviewing papers and submitting review articles and editorials over five years. A story about the case appears at www.theheart.org/article/786165.do.

Obituary:

Patricia Delaney, FDA Liaison To Cancer Patient Advocates

By Kirsten Boyd Goldberg

Patricia Delaney, assistant director of the Cancer Liaison Program in the FDA Office of Special Health Issues, died June 2 at Washington Hospital Center of acute myelogenous leukemia. She was 65 and lived in Washington, D.C.

Delaney was a 20-year survivor of stage IV

Hodgkin's disease and had dedicated the years since her diagnosis to public education about cancer clinical trials. She wrote and spoke frequently about her participation in an NCI clinical trial, using her experience to educate and advocate for cancer patients and their caregivers on access to clinical trials and potential therapies to extend life.

"I had tumors in six sites including my liver. And yet, as grave as this sounded to me, the doctors were telling me that I had a 75 to 80 percent likelihood of being cured," Delaney wrote in an article in Coping magazine in 1997. "How could there be a cure? I was told that for 20 years, cancer researchers had been conducting Hodgkin's disease clinical trials which resulted in not one, but two effective treatments for Hodgkin's disease.

"I resolved that if I was lucky enough to be cured, I would spend my time educating anyone who would listen to me about cancer clinical trials," she wrote.

Delaney authored many articles on clinical trials and cancer survivorship which were published widely in newspapers, magazines, and journals, including The Washington Post, the Journal of the American Medical Association, the Oncology Nursing Journal, Coping magazine and the Journal of the National Cancer Institute.

Delaney was born in Chicago and attended Barat College in Lake Forest, Ill. She taught elementary students in the Chicago public school system. In 1969, she moved to Washington, where she worked in leadership roles in the Head Start Bureau of the Department of Health, Education and Welfare, now the Department of Health and Human Services. She worked in Head Start's Indian and migrant program from 1969-1972.

From 1972-1981, she worked for Family Health Care Inc., a management and health policy consulting firm. She eventually became the company's president and chief executive officer. Later she began her own healthcare consulting company.

In 1987, Delaney was diagnosed with Hodgkin's disease and began treatment. She enrolled in a clinical trial at NCI comparing the standard MOPP regimen to MOPP plus four other drugs; the therapies turned out to provide equivalent benefit. In 1990, she returned to work at the HHS Health Resources and Services Administration, in the Office of Communications, Bureau of AIDS.

In 1994, she began working in the FDA Office of Special Health Issues at a time when cancer patient advocacy groups began to emerge as a important players in drug development and drug approval.

"She was a true public servant and an advocate for cancer patients," said Theresa Toigo, FDA assistant commissioner for special health issues, who hired Delaney to help start the Cancer Liaison Program. "Patty made us all deal with issues that would have been easier to overlook. She was relentless on behalf of patients."

At the oftentimes secretive agency, Delaney was a perpetual communicator, a link with the outside world. Informally, she made connections between people who she thought needed to talk with each other, helping patients obtain experimental treatments, connecting reporters with advocates, and offering guidance when other FDA officials were unwilling or unable to speak forthrightly.

Delaney was proud to say that she returned all calls, even those from Wall Street analysts fishing for clues about drug approval. They were constituents, and while they weren't entitled to answers, they were entitled to respect, she said.

Gestures of respect were important to Delaney. To her, it was imperative that advisory committee members listen attentively to patients testifying at the Oncologic Drugs Advisory Committee or taking part in its deliberations.

Last December, she fought to get into what was initially an invitation-only NCI workshop exploring the tumor promotion effect of erythropoiesis-stimulating agents. She thought it was critical that there be open public discussion about the science surrounding ESA safety issues.

Delaney's husband Douglas Klafehn died in 2006. She is survived by a son, Patrick Klafehn, of Washington, D.C.; a sister, Mary McGuire, of Chevy Chase, Md.; a brother, George Delaney, of Irvine, Calif., and many nieces and nephews.

Cancer Advocacy:

Mass. Democrats, NCCS To Provide Cancer Information

The National Coalition for Cancer Survivorship said it will provide free patient education materials and program information throughout Massachusetts.

The Massachusetts Democratic Party informed NCCS of its intention to create and distribute bracelets inscribed with "TEDSTRONG" as a show of support for Sen. Edward Kennedy (D-Mass.) as he moves forward with his cancer treatment. Any donations received from the distribution of the bracelets, which will be given out to delegates attending the Massachusetts State

Democratic Convention on June 7, will go to benefit NCCS to help the organization further its charitable activities through the distribution of free education materials to people diagnosed with cancer.

"Since he first entered the Senate, Senator Kennedy has been a national champion for quality cancer care," said Robert Sachs, chairman of the NCCS Board of Directors, and a 21-year cancer survivor.

"As Senator Kennedy deals with personal health challenges of his own, we are proud to stand with him in this battle and to support his legislative efforts to bring quality cancer care to all Americans," said Sachs, who is also a trustee of the Dana-Farber Cancer Institute and a Boston resident.

NCCS will coordinate with cancer care centers, hospitals, advocacy and support organizations in the state to distribute the Cancer Survival Toolbox, an award-winning self-learning audio program developed by NCCS in collaboration with the Oncology Nursing Society, the Association of Oncology Social Workers, and the National Association of Social Workers.

The Toolbox, provided free of charge, assists cancer survivors in getting information and building the skills they need to better meet and understand the challenges of their illness.

"The Cancer Survival Toolbox is a comprehensive and practical program that we developed to answer the complex questions people have when confronted with cancer," said Ellen Stovall, 36-year cancer survivor and NCCS president and CEO. "NCCS looks forward to putting the Toolbox in the hands of people diagnosed with cancer throughout the Commonwealth of Massachusetts in honor of Sen. Kennedy—a longtime friend to many cancer support and advocacy organizations across the country, a champion of healthcare issues, and a fervent leader in support of cancer quality improvement. We are proud to continue the work we've been doing with Sen. Kennedy for over two decades to advocate for quality cancer care for all Americans."

In the Cancer Centers:

CMS To Recognize NCCN's Drug Compendium For Part B

CENTERS FOR MEDICARE & MEDICAID SERVICES said it will recognize the **National Comprehensive Cancer Network** Drugs & Biologics Compendium as an additional source of information to determine which drugs may be covered under Medicare Part B to treat patients undergoing chemotherapy.

CMS said it will cease use of the American Medical Association Drug Evaluations compendium, which has not been published since 1995.

"We use these compendia to ensure that that Medicare beneficiaries can be assured that the Medicare contractors and their physicians have the most up-to-date drug information and the best available treatment options," said CMS Acting Administrator **Kerry Weems**. "This is important because today's ever-expanding industry of drug treatments is dynamic, requiring the constant monitoring and assessment of new interventions."

A compendium is a comprehensive listing of FDA-approved drugs and biologics. In some cases, compendia specialize in a particular subset of drugs, such as those used for anti-cancer treatment. Compendia include a summary of how each drug works in the body, as well as information for health care practitioners about proper dosing and whether the drug is recommended or endorsed for use in treating a specific disease.

The Medicare local contractors, who process and pay Medicare claims and approve coverage for drugs under Medicare Part B, use compendia as one of several tools to determine whether an anti-cancer drug should be covered under Medicare Part B.

Further information about CMS compendium decisions is available at http://www.cms.hhs.gov/CoverageGenInfo/02_compendia.asp.

FOX CHASE CANCER CENTER named **Eric Horwitz** acting chairman of the department of radiation oncology. Horwitz, the department's vice chairman and clinical director, replaces **Alan Pollack**, who became chairman of the radiation oncology department at the University of Miami after serving Fox Chase as chairman for seven years. Since joining Fox Chase in 1997, Horwitz developed advanced treatment programs using intensity-modulated radiation therapy (IMRT), image-guided radiation therapy and brachytherapy, including high-dose-rate brachytherapy for prostate cancer. . . . **DAVID LYNDEN** was named the Stavros S. Niarchos Associate Professor in Pediatric Cardiology at Weill Cornell Medical College, where he is investigator in the Division of Pediatric Hematology and Oncology and associate professor of cell and development biology. Lyden also is assistant attending in pediatrics at Memorial Sloan-Kettering Cancer Center. "David's pioneering work in vascular biology and cardiology has provided great insights in the treatment of vascular diseases and cancer, and his findings have had numerous clinical implications," said **Gerald Loughlin**, chairman of the Department of Pediatrics at Weill Cornell.

NIH News:

NIH Director Announces Changes To Peer Review

An NIH committee studying the institutes' peer review system presented a report with a set of comprehensive recommendations to NIH Director Elias Zerhouni at a meeting this week of the Advisory Committee to the Director.

The committee has been deliberating for a year on ways to improve peer review. An important component of the new plan is an increased commitment to investigator initiated high-risk, high-impact research to prevent a slowdown of transformative research, despite difficult budgetary times.

"The scientific community became truly engaged in this comprehensive effort to figure out how to make peer review work better for both the reviewers and the applicants," Zerhouni said. "The results of this collective effort are concrete solutions that will maximize flexibility, remove any unnecessary burden, stimulate new innovation, and promote transformative research."

The initiatives were presented to the ACD by Lawrence Tabak, director of the National Institute of Dental and Craniofacial Research and co-chairman of the two peer review working groups.

A comprehensive framework was created and implementation will be carried out over the next 18 months, NIH officials said.

Four Main Priorities

The Implementation Plan Report consists of four main priorities. Highlights include:

—Priority 1 - Engage the Best Reviewers: Increase flexibility of service, formally acknowledge reviewer efforts, further compensate time and effort, and enhance and standardize training

—Priority 2 - Improve Quality and Transparency of Reviews: Shorten and redesign applications to highlight impact and to allow alignment of the application, review and summary statement with five explicit review criteria, and modify the rating system

—Priority 3 - Ensure Balanced and Fair Reviews Across Scientific Fields and Career Stages

—Support a minimum number of early stage investigators and investigators new to NIH, and emphasize retrospective accomplishments of experienced investigators

—Encourage and expand the Transformative Research Pathway

—Create a new investigator-initiated Transformative R01 Award program funded within the NIH Roadmap with an intended commitment of a minimum of $250 million over five years

—Continue the commitment of -- and possibly expand the use of -- the Pioneer, EUREKA, and New Innovator Awards. NIH will invest at least $750 million in these three programs over the next 5 years.

—Reduce the burden of multiple rounds of resubmission for the same application, especially for highly meritorious applications

—Priority 4 - Develop a Permanent Process for Continuous Review of Peer Review

"As we contemplated possible changes, we were guided by several fundamental principles," Zerhouni said. "First, while improving the system, do no harm. That is, ensure that any changes to the peer review system bring significant value and outweigh costs.

"Second, continue to maximize the freedom of scientists to pursue high-risk, high-impact research," Zerhouni said. "Moreover, we want to cultivate a sense that we continuously re-evaluate the peer review system to ensure that it is the best that it can be."

Further information about the implementation plan is available at http://enhancing-peer-review.nih.gov.

Funding Opportunities:

RFA-MD-08-004: NCMHD Exploratory Centers of Excellence. P20. Letters of Intent Receipt Date: July 1. Application Receipt Date: July 31. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-MD-08-004.html. Inquiries: Derrick Tabor, 301-402-1366; tabord@mail.nih.gov.

RFA-MD-08-005: NCMHD Comprehensive Centers of Excellence. P60. Letters of Intent Receipt Date: July 30. Application Receipt Date: Aug. 29. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-MD-08-005.html. Inquiries: Nathan Stinson, Jr., 301-402-1366; stinsonn@mail.nih.gov.

RFP S08-184: Nanotheraperapeutics. Response Due date: June 27. Full text: http://www.fbodaily.com/archive/2008/06-June/06-Jun-2008/FBO-01586888.htm. Inquiries: Shannon Jackson, 301-228-4022; sjackson@mail.ncifcrf.gov.

RFP N02-RC-81020-56: Patient Recruitment. Full text: http://www.fbodaily.com/archive/2008/05-May/21-May-2008/FBO-01576039.htm. Inquiries: Juana Diaz, 301-496-8613; diazj@mail.nih.gov. and Richard Hartmann 301-496-8620; Richard.Hartmann@nih.gov.

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THE CANCER LETTER

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Business & Regulatory Report

Product Approvals & Applications:

ODAC Votes Unanimously In Favor Of GSK's Promacta For Chronic ITP

The FDA Oncologic Drugs Advisory Committee unanimously voted 16-0 that Promacta (eltrombopag, sponsored by GlaxoSmithKline) demonstrated a favorable risk-benefit profile for the short-term treatment of patients with chronic idiopathic thrombocytopenic purpura.

The FDA advisory committee was held May 30 at the 2008 American Society of Clinical Oncology annual meeting in Chicago.

The advisory committee reviewed studies evaluating the safety and efficacy of eltrombopag in the short-term setting. Clinical data were presented

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Deals & Collaborations:

National Mesothelioma Virtual Bank To Provide Annotated Tissue Samples

A newly-created **National Mesothelioma Virtual Bank** will provide mesothelioma tissue samples from institutions, clinically annotated in an accessible database, to researchers in mesothelioma investigations.

"This is a great accomplishment for the meso community," said Christopher Hahn, executive director of the Mesothelioma Applied Research Foundation. "We have long advocated for federal research funding and the creation of a mesothelioma tissue bank. It is an important resource, expected to greatly advance the genetic and protein profiling of the meso cancer cell."

The NMVB is a result of the collaboration of multiple organizations, the group said. The Center for Disease Control and Prevention, in association with the National Institute for Occupational Safety and Health, provided the initial $1 million grant to Michael Becich at the **University of Pittsburgh Medical Center** to begin the tissue bank. Others credited with creating the bank include: Harvey Pass, of New York University Medical Center, and Steven Albelda, of University of Pennsylvania Medical Center, both members of the Meso Foundation.

Canary Foundation, of San Jose, Calif., and the **NCI Early Detection Research Network** said they are forming a partnership to identify and validate biomarkers of high-risk prostate cancer within the context of an active surveillance study.

The goal of the collaboration is to reduce over-treatment by identifying

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Promacta, An Oral Treament For ITP, Gets ODAC 16-0 Vote

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and discussed that support eltrombopag increased platelet counts and reduced bleeding.

"Chronic ITP is a condition, which can have serious complications and be life threatening. Two of the most fundamental endpoints are crucial to managing this disease—improved platelet counts and decreased bleeding," said Paolo Paoletti, senior vice president of the Oncology Medicine Development Center at GSK. "If approved, this would make the drug a potential new clinical option that can address a true unmet medical need. An FDA approval for eltrombopag would represent an important development for these patients and would make the medication the first oral treatment of its kind for this disease. We look forward to working with the agency to achieve that goal."

FDA recently granted eltrombopag orphan drug designation for this indication.

Eltrombopag is a once-daily oral treatment to induce the production of cells in the bone marrow to increase platelets, which are critical in minimizing the incidence of bleeding in chronic ITP. If approved, it would be the first oral short-term treatment of previously treated patients with chronic ITP to increase platelet counts and reduce or prevent bleeding.

In the pivotal studies, the most common adverse events observed in patients taking eltrombopag were headache, nasopharyngitis, and nausea.

The NDA submission was supported by the largest database of clinical trial information on investigational therapies for chronic ITP patients. Two pivotal trials—one phase III trial and one phase II trial—were submitted.

Chronic ITP is a disorder marked by increased platelet destruction and/or inadequate platelet production in the blood, which causes an increased risk of bruising and bleeding. There are estimated to be approximately 60,000 individuals diagnosed with chronic ITP in the U.S. People with chronic ITP often bleed from small blood vessels causing bruises, nosebleeds or even fatal gastrointestinal or intra cerebral bleeds, although these are rare.

Eltrombopag is an oral, non-peptide thrombopoietin receptor agonist that has been shown in pre-clinical research and clinical trials to stimulate the proliferation and differentiation of megakaryocytes, the bone marrow cells that give rise to blood platelets. Eltrombopag was discovered as a result of research collaboration between GlaxoSmithKline and Ligand Pharmaceuticals.

Cell Therapeutics Inc. (NASDAQ: CTIC; MTA) of Seattle said it received a positive opinion from the European Medicines Agency for the brand name Opaxio (paclitaxel poliglumex), which would replace the brand name Xyotax.

In April, the EMEA accepted for review the CTI Marketing Authorization Application for the agent in non-small cell lung cancer with ECOG performance status 2, the company said.

Opaxio is an investigational, biologically enhanced, chemotherapeutic that links paclitaxel to a biodegradable polyglutamate polymer.

Dilon Technologies of Newport News, Va., said it has received Conformite Europeenne Mark approval for the commercial sale of the Dilon 6800 Gamma Camera in the European Union.

The Dilon system is a high-resolution gamma camera that allows for molecular imaging of the breast and other small organs for early cancer detection, the company said.

S*BIO Pte Ltd of Singapore said FDA granted Orphan Drug designation to SB1518 in myeloproliferative disorders.

Preclinical data demonstrated anti-proliferative and anti-tumor activity, combined with tolerability of the JAK2 inhibitor, the company said.

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SB1518 is an orally active small molecule JAK2-selective kinase inhibitor against both the wild type JAK2 kinase and the JAK2 kinase with the V617F mutation, the company said.

Vaccinogen Inc. of Frederick, Md., said Dutch health authorities have authorized the company to manufacture its OncoVAX anti-colon cancer vaccine.

The Dutch approval of the Vaccinogen facility based in Emmen, The Netherlands, also paves the way to its pivotal phase IIIb clinical trial,

"The facility in Emmen, The Netherlands, can produce up to 3,500 vaccines annually, equivalent to $130 million in revenues," said Michael Hanna, CEO at Vaccinogen. "That number only scratches the surface of demand for a stage II colon cancer vaccine. One of every three patients who have their cancer removed see it return--and the results are usually fatal. Our experience with OncoVAX has resulted in increasing the patients' chance of survival by more than 50 percent,"

The Dutch license permits the company to commercialize the vaccine.

Watson Pharmaceuticals Inc. (NYSE:WPI) of Corona, Calif., said FDA has approved Mixject, the delivery system for Trelstar (triptorelin pamoate for injectable suspension), a palliative treatment for advanced prostate cancer.

Mixject, developed and manufactured by Medimop Medical Projects Ltd., a subsidiary of West Pharmaceutical Services Inc., combines Trelstar DEPOT 3.75 mg and Trelstar LA 11.25 mg with features that make preparation, administration and disposal easier, the company said.

Deals & Collaborations:

EDRN Study To Find, Validate Prostate Cancer Biomarkers

(Continued from page 1)

aggressive versus passive tumors, the groups said. The Canary Foundation will provide funding for a Prostate Active Surveillance Study at six institutions, the foundation said.

EDRN will establish disease-specific Common Data Elements, a biospecimen management system and a protocol oversight program to expedite the storage and processing of patient information and biological specimens. Also, the Canary Foundation and EDRN said they would establish a Biomarker Evaluation Group to determine those biomarkers that are most promising for evaluation using the biologic materials collected by the Canary Prostate Consortium.

"With prostate cancer being one of the major focus areas for Canary's cancer programs and with the EDRN multiple ongoing studies related to the early detection of prostate cancer, we see this as a complementary and significant partnership," said Sudhir Srivastava, chief of the Cancer Biomarkers Research Group at NCI.

Six institutions will participate in the active surveillance study including Stanford University, University of California, San Francisco, University of British Columbia, University of Washington Fred Hutchinson Cancer Research Center in Seattle and the University of Texas Health Science Center, San Antonio.

The Canary prostate team is headed by Peter Nelson, member of the Human Biology and Clinical Research Divisions, Fred Hutchinson Cancer Research Center and professor of oncology, Department of Medicine at the University of Washington.

Champions Biotechnology Inc. of Arlington, Va., said it has made an agreement with **ImClone Systems Inc.** for the preclinical evaluation of therapeutic antibodies in the ImClone clinical development pipeline.

Under the agreement, ImClone will use the Champions Biotechnology Biomerk Tumorgrafts in the preclinical evaluation, the company said.

EUSA Pharma Inc. of Doylestown, Penn., said it has completed its acquisition of **Cytogen Corp**. following the approval of the Cytogen shareholders at a special meeting in early May.

Under the agreement, Cytogen shareholders will receive $0.62 per share, valuing the company at $22.6 million. To meet the consideration, EUSA said it has raised $50 million in an investment round led by TVM Capital and supported by the EUSA investors, Essex Woodlands, 3i, Goldman Sachs, Advent Venture Partners, SV Life Sciences, NeoMed and NovaQuest.

The acquisition brings three oncology and pain control products to EUSA, a U.S. specialty sales force and an established commercial infrastructure, the company said. The products include Caphosol for oral mucositis, ProstaScint for prostate cancer, Quadramet for pain in cancer that has spread to the bones.

NGN Capital said the newly formed **ACT Biotech Inc.** has entered into a license agreement with **Bayer HealthCare LLC** for a portfolio of clinical

and early stage oncology assets. In conjunction with the agreement, ACT has raised $12 million in the first tranche of a Series A financing led by NGN Capital, the company said.

NGN is a New York-based healthcare venture capital investment firm. Under the license agreement with Bayer, San Francisco-based ACT Biotech has acquired an anti-angiogenic receptor tyrosine kinase inhibitor entering phase II studies for colorectal cancer.

An additional program in-licensed is a first-in-class multi-mode kinase inhibitor in late preclinical stage with application in different cancer types. The company said it also acquired additional preclinical stage programs in oncology.

The company will continue to cooperate with the Melanoma Therapeutics Foundation, which is a co-founder in ACT Biotech.

Oncothyreon Inc. (NASDAQ: ONTY) (TSX: ONY) of Bellevue, Wash., said it has completed the transfer of assays and manufacturing technology for Stimuvax (BLP25 liposome vaccine) to **Merck KGaA** of Darmstadt, Germany, triggering a payment to Oncothyreon of $3 million.

The payment will be made under the terms of the amended and restated supply agreement signed in 2007.

Stimuvax is an investigational therapeutic cancer vaccine that induces an immune response to cancer cells that express MUC1, a glycoprotein antigen, the company said.

Merck KGaA is conducting a phase III trial of Stimuvax known as the Stimulating Targeted Antigenic Responses To NSCLC.

START is a randomized, double-blind, placebo-controlled 1300-patient study in unresectable stage III NSCLC with response or stable disease after at least two cycles of platinum based chemo-radiotherapy, the company said.

Siemens Healthcare of Deerfield, Il., and **Laboratory Corporation of America Holdings** said they have entered a non-exclusive agreement to develop diagnostic tests in companion diagnostics, metabolic syndrome, oncology and diabetes.

Companion diagnostics identify the suitability between patients and a particular drug therapy, the companies said. The tests can be used in personalized medicine to improve safety and efficacy of therapeutic drugs and to determine individual dosing.

The collaboration brings the Siemens products and services used for diagnosing medical conditions and monitoring patient therapy and the LabCorp reference laboratory of 220,000 clients in the U.S. Together, the companies said they would develop and introduce diagnostic tests to advance care through early detection and proper monitoring of disease.

Takeda Pharmaceutical Company Ltd., of Osaka, Japan, and **Millennium Pharmaceuticals Inc**. (NASDAQ:MLNM) of Cambridge, Mass., said Takeda has completed a cash tender offer by its subsidiary, Mahogany Acquisition Corp., to acquire all outstanding shares of Millennium common stock for $25 per share.

Takeda also said it has begun an offering period to acquire all of the remaining untendered shares. After expiration of the subsequent offering period, Takeda plans to complete its acquisition of Millennium by means of a merger under Delaware law.

Upon completion of the merger, Millennium will become an indirect wholly-owned subsidiary of Takeda, and Millennium common stock will cease to be traded on NASDAQ, the company said.

Millennium markets the cancer drug Velcade as well as a clinical development pipeline of product candidates.

Tigris Pharmaceuticals Inc. of Bonita Springs, Fla., said it has signed a CRADA with NCI to collaborate on clinical and preclinical development of AFP-464, an aminoflavone in phase I development.

AFP-464 is converted to metabolites, which bind covalently to DNA, resulting in p53 activation and apoptosis, the company said.

The CRADA is part of a four-year collaboration encompassing multiple phase I and phase II studies with correlating translational research of AFP-464 in a variety of tumor types, the company said.

Under the CRADA, two phase I studies with AFP-464 sponsored by NCI, are enrolling in the U.S., at sites including Mayo Clinic, Wayne State University, and the University of Maryland. The studies are evaluating the product in advanced solid tumors. Tigris said it also began a phase I program in Belgium and France; this work is not included in the CRADA research.

Transgenomic Inc. (BULLETIN BOARD: TBIO) of Omaha said NCI has approved a proposal to perform mutational analysis and sequencing of the mitochondrial genes in the NCI 60 cancer cell line panel.

Mitochondrial damage is an early warning signal in different cancers, the company said.

"Tens of thousands of compounds have been tested against the NCI 60 cell lines in the NCI pharmacological database of cancer drugs," said Eric Kaldjian, chief scientific officer at Transgenomic Inc. "This collaboration makes it possible to test whether in vitro responses to anti-cancer agents are linked to alterations in the mitochondrial genome and can be detected with our sensitive mutation detection technology."

Clinical Trials:

Phase III Trial Of GSK's Tykerb In Early Breast Cancer Begins

GlaxoSmithKline and **Breast International Group**, a Brussels-based academic breast cancer research network and one of its member groups, the **Spanish Breast Cancer Cooperative Group**, said they have begun a global phase III study of Tykerb in early breast cancer.

The Neoadjuvant Lapatinib and/or Trastuzumab Treatment Optimization study, or Neo-ALTTO, will evaluate and compare the rate at which cancer cells disappear in the breast following treatment with Tykerb (lapatinib) and/or Herceptin (trastuzumab) before surgery in early-stage HER2-positive breast cancer.

Tykerb is an oral small-molecule inhibitor of the HER2 tyrosine kinase receptor. Neo-ALTTO is a three-arm, randomized, multi-center, open-label study. After treatment with Tykerb for six weeks, the same targeted therapy will be repeated for 12 weeks with the addition of paclitaxel. Surgery will be performed on all patients, after which each will receive three courses of chemotherapy followed by the same targeted therapy for 34 weeks.

The primary endpoint is the rate of pathological complete response at the time of surgery as well as understand the biological difference of the three treatment regimens using a neoadjuvant approach. Secondary endpoints include measurements of safety and tolerability, tumor response rate, disease-free survival and overall survival. Target enrollment is 450 with 130 clinical trial centers participating in 26 countries.

SOLTI, a non-for-profit organization under Spanish law, is a network of 30 medical oncology departments from university hospitals across Spain and Portugal. The mission of SOLTI is to encourage, design and develop clinical trials in breast cancer and in other solid tumors to answer questions about cancer treatment.

ImClone Systems Inc. (NASDAQ:IMCL) said a phase II trial of IMC-A12, its fully human, IgG1 anti-insulin-like growth factor-1 receptor (IGF-1R) monoclonal antibody for advanced hepatocellular cancer has opened for enrollment at Memorial Sloan-Kettering Cancer Center.

The study is a component of ten phase I and phase II trials of the drug sponsored by the NCI Cancer Therapy Evaluation Program.

The 50-patient study will enroll patients who had received local therapy, including surgery, radiofrequency ablation, radiotherapy, and percutaneous intratumoral treatment, but had not received prior systemic therapy except for sorafenib tosylate. The study would assess, the safety, efficacy and biological behavior of IMC-A12 administered weekly by intravenous infusion.

IMC-A12, a fully human IgG1 monoclonal antibody, targets the human IGF-1R, thereby inhibiting IGFs I and II from binding to and activating the receptor, the company said.

BiPar Sciences Inc. Brisbane, Calif., said it has expanded the phase II trial programs for BSI-201 in ovarian cancer.

The company said it is evaluating the agent, the first poly ADP-ribose polymerase inhibitor in its DNA repair portfolio, as a monotherapy for ovarian cancer with a mutation in the BRCA1 or BRCA2 genes.

"We believe BSI-201 holds great promise as a targeted therapy in this difficult-to-treat type of ovarian cancer," said Carol Aghajanian, co-principal investigator and chief of the gynecologic medical oncology service at Memorial Sloan-Kettering Cancer Center. "BRCA-negative patients are at higher risk of breast and ovarian cancer because BRCA plays a key role in repairing DNA errors that lead to tumor formation."

The company said it is conducting a phase II trial of BSI-201 in triple- negative breast cancer and is collaborating with the New Approaches to Brain Tumor Therapy consortium, an NCI-funded research group, to test the product BSI-201 in glioblastoma multiforme. An additional trial in uterine cancer will begin enrollment soon.

EntreMed Inc. (NASDAQ:ENMD) said **Dana-Farber Cancer Institute** has joined the **University of Colorado Cancer Center** in conducting a phase I study of ENMD-2076 in advanced cancer.

ENMD-2076 is a selective kinase inhibitor with

activity against Aurora A and tyrosine kinases linked to the promotion of cancer and inflammatory diseases, the company said. Geoffrey Shapiro, of Dana-Farber, and Wells Messersmith, of the University of Colorado, are co-principal investigators.

Oncolytics Biotech Inc. (TSX:ONC, NASDAQ: ONCY) of Calgary said it has begun enrolment in a clinical trial using intravenous administration of Reolysin in combination with cyclophosphamide, a chemotherapeutic agent as well as an immune modulator, in advanced cancers.

James Spicer, of King's College in London, Johann de Bono and Kevin Harrington, of The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research, London and Hardev Pandha, of the Royal Surrey County Hospital NHS Trust, Surrey and Mount Alvernia Hospitals, are principle investigators.

The REO 012 trial is an open-label, dose-escalating, non-randomized trial of Reolysin given intravenously with escalating doses of cyclophosphamide.

Pathwork Diagnostics Inc. of Sunnyvale, Calif., said **Stanford University School of Medicine** has begun an investigational study of the Pathwork Tissue of Origin Test.

The test uses genomics-based technology to determine the origin of a tumor to optimize cancer-specific treatment, the company said. The study will evaluate the ability of the test to diagnose hard-to-identify tumors, with test samples processed at the Stanford University School of Medicine laboratory, the company said.

Stanford participated in a cross-laboratory comparison study of the Pathwork Tissue of Origin Test in 60 metastatic and poorly differentiated and undifferentiated tissue specimens. The test demonstrated an average 94 percent overall concordance across four laboratories.

The test measures the expression of 1,500 genes in order to compare the gene expression profile of a tumor to those of 15 known tissues representing more than 60 morphologies.

The test then provides a report with an objective, probability-based score for each tissue, the company said. The test uses a proprietary Pathchip microarray and runs on the Affymetrix GeneChip System. In a clinical validation study of 477 metastatic and poorly differentiated and undifferentiated tumors, which had already been identified using available methodologies, the test demonstrated a sensitivity of 89 percent and a specificity of 99 percent, the company said.

Progen Pharmaceuticals Ltd. (NASDAQ: PGLA) of Brisbane said it has resumed enrolment at the University of Chicago in the phase I dose-escalation study of PG-11047 in advanced cancer.

Progen said it is developing PG-11047 (formerly CGC-11047), following its acquisition of Cellgate Inc. earlier this year. Under CellGate, the trial had recruited 31 patients and had shown little evidence of toxicity, while using higher doses than most studies of polyamine compounds.

The trial would assess the maximum tolerated dose of the agent, the company said.

Data from the trial will be used in parallel with a separate PG-11047 study assessing the agent in combination with other marketed anti-cancer drugs as the basis for determining phase II development, the company said. About PG-11047:

PG-11047 is a polyamine analogue, which modifies the production of natural polyamines.

Quantum Immunologics Inc. of Tampa said it has begun a phase I/II trial to assess the safety and efficacy of an anti-cancer vaccine/immunotherapy in stage IV advanced breast cancer.

The immuno-therapeutic vaccine developed by the University of South Alabama would activate the immune system against a cancer-specific protein to destroy the cancer cells, the company said.

The immunizing protein, called the Oncofetal Antigen or immature Laminin Receptor Protein, is a universal cancer antigen or protein expressed in all human cancer types tested by USA, the company said.

Patients with disseminated breast carcinomas and meeting the clinical trial entrance criteria will be treated at the Southern Cancer Center in collaboration with the Providence Cancer Center and other local oncology centers in and around Mobile, the company said.

Investigators will take blood samples and expose Dendritic Cells in vitro to replicated iLRP, cultured, and reintroduce them via subdermal injection. The iLRP-sensitized DC will then recognize iLRP as a foreign protein or antigen on cancer cells and, when reintroduced into the body, will then, in turn, sensitize or introduce T-killer lymphocytes to the iLRP protein. Once the killer cells are activated against the iLRP protein on the cancer cells, they would destroy the breast cancer.

In an Austrian study, 11 advanced renal cell carcinoma patients who failed conventional therapy were treated with the immunotherapy. They developed

a cytotoxic response secondary to activation of their T-killer cells against the iLRP protein using the same type of technique as in the present study. Five of the 11 are alive with a median follow up of 46.7 months (range 33-54 months). The one-year survival rate was 90 percent; two-year survival rate 54 percent; three-year survival rate 45 percent. No serious side effects occurred and most were flu-like symptoms secondary to the immune response. This study is designed to determine whether breast cancer patients will respond similarly and without toxicity, the company said.

The three senior immunobiologists, Joseph Coggin, Jim Rohrer and Adel Barsoum, Department of Microbiology and Immunology at the University of South Alabama, will collaborate with the primary investigator, Paul Schwartzenberger, SCC oncologist.

Saladax Biomedical Inc. of Bethlehem, Penn., said a study of blood-based 5-FU dose management with the Folfox regimen will use its Personalized Chemotherapy Management, an immunoassay based on a patented technology.

The assay provides LC-MS-like performance but is easier to use and less expensive, the company said.

The multicenter, randomized phase III 200-patient study for metastatic colorectal cancer will determine the efficacy of 5-FU dose management utilizing the PCM test. Edward Chu, chief of medical oncology and deputy director of the Yale Cancer Center, is lead investigator. The study will involve other cancer centers in the U.S., as well as the Paul Papin Cancer Center in France.

Sunesis Pharmaceuticals Inc. (NASDAQ:SNSS) of South San Francisco said it has begun the Response Evaluation of Voreloxin in Elderly AML, or REVEAL-1, phase II trial of voreloxin (also known as SNS-595).

Enrollment and treatment has begun at the Indiana University Melvin and Bren Simon Cancer Center under Larry Cripe, associate professor, Department of Medicine, Division of Hematology and Oncology, Indiana University School of Medicine.

The open-label, multi-center trial would evaluate the anti-leukemic activity of voreloxin as a single agent, measured as either complete remission or complete remission without full platelet recovery. The 55-patient study also will measure the duration of the responses. Participants must be at least age 60 with untreated AML and satisfy at least one of the following factors: poor performance status; intermediate or unfavorable cytogenetics; prior antecedent hematologic disorder; or age greater than or equal to 70 years. Treatment consists of three weekly doses of 72 mg/m2 of voreloxin in a treatment cycle.

Sunesis said results from its phase I single agent dose-escalation study in relapsed or refractory AML demonstrated 13 of 30 patients, or 43 percent, who received doses of voreloxin of 50 mg/m2 or greater on a weekly dose schedule, achieved bone marrow blast reductions to less than five percent. The company said five of the 13 achieved either CR, CRp or complete remission with incomplete recovery of normal hematopoietic blood elements. Voreloxin was well tolerated, with a dose-limiting toxicity of reversible oral mucositis. A maximum- tolerated weekly dose of 72 mg/m2 was established.

Voreloxin is a naphthyridine analog, structurally related to quinolones, that both intercalates DNA and inhibits topoisomerase II, resulting in replication-dependent, site- selective DNA damage, irreversible G2 arrest and rapid apoptosis, the company said.

Telik Inc. (NASDAQ:TELK) of Palo Alto said it has begun two phase II studies, one with Telintra tablets in myelodysplastic syndrome, and a second with the tablets in cancer with chemotherapy-induced neutropenia.

Telik said it completed a 65-patient phase II study with the IV formulation of the agent in MDS, and a dose-escalating phase I 45-patient study of the oral formulation of the tablets.

The randomized phase II 86-patient study with Telintra tablets would consist of two dose schedules of the tablets in low-to-intermediate risk MDS. The study would determine the hematologic improvement rate in erythroid or red blood cell precursors in each treatment group as assessed by the International Working Group criteria.

One group will be given a starting dose of 4500mg daily in divided doses for two weeks followed by one week off therapy. The second group will receive the same dose of Telintra for three weeks followed by one week off therapy. Treatment will continue for up to six months, and if clinical benefits continue, it may be extended for an additional six months with continuous daily dosing.

The second randomized phase II study with Telintra tablets will be conducted in non-small cell lung cancer being treated with standard front line combination chemotherapy, the company said.

A randomized phase II study with Telintra tablets in CIN would enroll 135 patients. One group of 90 patients will receive chemotherapy followed the next day by a

starting dose of 4500mg of Telintra per day in twice daily divided doses until white blood cell count recovery. Another group of 45 will be the chemotherapy-alone control group, which will receive standard supportive care following chemotherapy. The study would evaluate the effect of oral Telintra on accelerating hematologic recovery from chemotherapy.

VION Pharmaceuticals Inc. (NASDAQ:VION) of New Haven, Conn., said an investigator-sponsored phase I/II trial of Cloretazine in combination with cytarabine in elderly patients with untreated acute myelogenous leukemia and high-risk myelodysplastic syndromes has begun.

The trial is being conducted under the direction of Ellen Ritchie at the Weill-Cornell Medical College. Co-investigators are Eric Feldman and Gail Roboz.

In the Courts:

Oncologist Pays Damages In Case Of Drug Importation

New York area oncologist Kee Shum and wife Li Shum agreed to pay $275,000 in damages to the federal government to resolve allegations that they violated the federal False Claims Act in connection with claims they submitted to the Medicare program for oncology drugs that were imported from Canada, prosecutors said.

The Shums also agreed to enter into an integrity agreement with the HHS to ensure that their medical practice, located in Flushing, Queens, is operated in a lawful manner in the future, officials said.

The settlement was announced by the office of the U.S. Attorney for Eastern District of New York, as well as officials from the HHS Office of Inspector General and the Federal Bureau of Investigation.

The government alleged that from October 2004 through October 2005, the defendants purchased oncology drugs that were imported from Canada, and then sought and received reimbursement from the Medicare program "despite knowing that the drugs were not subject to reimbursement," officials said in a statement.

The $275,000 settlement figure represents twice the amount of damages allegedly incurred by Medicare, the authorities said. In settling the case, the defendants have not admitted to engaging in the conduct alleged in the complaint.

The government began its investigation after another physician filed suit in the Eastern District of New York on behalf of the U.S. government.

The whistleblower, Suby Rao, a Chicago area hematologist and oncologist, alleged that doctors throughout the U.S. were importing oncology drugs from Canada because they could be purchased at a lower price than domestic oncology drugs. As a result, doctors could increase profit margins when they sought reimbursement from federal insurance programs.

The complaint alleges that the patients were generally not informed that they were being administered an imported drug. Under the federal False Claims Act, a private individual who has uncovered fraud against the government may file a suit on behalf of the United States. If the government is successful in resolving or litigating those claims, the person who originally made the allegations may share in part of the recovery.

"By participating in the scheme, doctors risked the health and safety of their cancer patients by buying drugs that may have been counterfeit or contaminated," Colette Matzzie, attorney with Phillips & Cohen, a Washington, D.C., firm which represents the whistleblower Rao, said in a statement. "We hope that the settlement with Dr. Shum is the first of many enforcement actions taken against doctors who illegally import oncology drugs."

Baptist Health South Florida Inc. of Miami has agreed to pay $7.8 million to settle claims that it violated the False Claims Act and the Stark Statute between 2003 and 2005, by paying compensation to an oncology group that was a source of patient referrals to two Baptist-owned facilities, the U.S. Department of Justice said.

Under the statute, Medicare providers like Baptist are prohibited from billing the federal health care program for referrals from doctors with whom the providers have a financial relationship, unless that relationship falls within certain exceptions.

According to DOJ, in 2006, Baptist submitted a report to the HHS Office of Inspector General, where it described a contract under which Oncology Hematology Group of South Florida, a community-based medical group, provided physics and dosimetry services to Baptist Hospital of Miami and South Miami Hospital, two facilities owned by Baptist. In its report, Baptist stated that for a period of time between 2003 and 2005, it had inadvertently run afoul of the Stark Statute by paying more than fair market value for services of the oncology group. Officials said the settlement resulted from the disclosure.

The case was handled by the Department of Justice Civil Division and the HHS Office of Inspector General.