THE CANCER LETTER

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Advisors Call For External Oversight, Coordination Of NCI Clinical Trials

By Kirsten Boyd Goldberg

Concluding that NCI's clinical trials system is wasteful and inefficient, a working group recommended an internal reorganization of the Institute and the appointment of a permanent external oversight committee for clinical trials.

"We feel that it will be impossible to organize clinical trials nationally unless NCI itself gets its house in order and is able to coordinate these activities from within, as well as from without," said NCI Division of Cancer Treatment and Diagnosis Director James Doroshow, who served as

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In Brief:

Eric Rowinsky, Philip Frost Join ImClone; Wilson Replaced As Cancer Panel Secretary

ERIC ROWINSKY was named senior vice president and chief medical officer at ImClone Systems Inc. and **Philip Frost** joined the company as executive vice president and chief scientific officer. Rowinsky is the former director of the Institute for Drug Development of the Cancer Therapy and Research Center in San Antonio and the SBC Endowed Chair for Early Drug Development at the IDD. Frost is the former vice president of oncology and co-director of the oncology therapeutic area leadership team at Wyeth. . . . **MAUREEN WILSON** stepped down as executive secretary of the President's Cancer Panel to devote more time to her job as NCI's ethics counselor, NCI Director **Andrew von Eschenbach** said. She has been the Panel's executive secretary since 1993, when she was appointed assistant director of NCI for ethics and the President's Cancer Panel. **Abby Sandler**, head of the Institute Review Office for NCI, was appointed executive secretary for the Panel. Wilson "never complained" and "worked tirelessly" for the Panel even as her duties as ethics officer became "enormous and complex" with Congressional inquires over the past year, von Eschenbach said to the National Cancer Advisory Board Feb. 16. The Panel meets four times a year. Its members are **LaSalle Leffall**, of Howard University College of Medicine; **Lance Armstrong**, founder of the Lance Armstrong Foundation; and **Margaret Kripke**, of M.D. Anderson Cancer Center. . . . **DANIELA GERHARD** has been named director of the NCI Office of Cancer Genomics. She joined NCI in 2002 and has served as acting director of OCG since 2003. . . . **JIMMIE HOLLAND** received the Claude Jacquillat Award for Clinical Cancer Research at the International Congress of Anti-Cancer Treatment

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Advisors Urge Standardization Of Clinical Research Tools

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co-chairman of the working group.

The National Cancer Advisory Board unanimously accepted the recommendations of the Clinical Trials Working Group at its Feb. 17 meeting.

Over the past decade, advisory committees and other organizations recommended specific changes in NCI's management of its clinical trials cooperative groups, resulting in limited pilot projects to reduce inefficiency. The report issued last week is the first to call for major reorganization within NCI as well as strong oversight from external experts.

"We are going to put full energy and full effort behind this, and bring this to fruition as rapidly as possible, because people who are suffering and dying out there… deserve nothing less than what this committee has told us we can and should do, and, therefore, we just will get on with it," NCI Director Andrew von Eschenbach said.

Von Eschenbach formed the working group in early 2004. The group's charge was to "take a blank sheet of paper and gaze into the future," he said to the NCAB last week.

"At the beginning, I think many people assumed that the blank sheet of paper with everything on the table meant that we were going to demolish everything," von Eschenbach said. "In fact, there is great value and very precious and important things that already are in place. So, it was really not a matter of demolishing. It became a matter of remodeling.

"There are parts of the system that we will have to demolish and radically change," he said. "There are parts of the system that we will build upon further and enhance and enrich. There are many parts of the system that need to be coordinated and integrated in a more efficient and effective way."

The report didn't specify how NCI should restructure, and Institute officials didn't discuss explicit plans. Currently, the Cancer Therapy Evaluation Program in DCTD coordinates the Institute-led treatment trials, while the Division of Cancer Prevention oversees prevention trials, and the Center for Cancer Research leads trials conducted by intramural researchers.

"Perhaps the most important of all of the recommendations that you've heard about this morning, because it parallels the potential empowerment of an extramural clinical trials advisory group, is to 'develop the necessary organizational structure within the NCI to coordinate the entire clinical trials enterprise supported by the Institute,' including the intramural program clinical trials activity," said DCTD Director Doroshow.

More specific plans and a budget for implementing the recommendations will be developed "over the next several months," Doroshow said.

The report made a total of 21 recommendations emphasizing standardization of research tools including case report forms, contracts, and common databases, as well as prioritization of trials and correlative studies.

"The clinical trials processes is extraordinarily complicated and extraordinarily inefficient," David Parkinson, vice president and head of the Clinical Oncology Therapeutic Area at Amgen and co-chairman of the working group's standardization and infrastructure subcommittee, said to the NCAB. "It requires the most time and the most resource utilization when it comes to the actual real-world development of new therapeutics. So the opportunities for introducing higher standards of performance and greater efficiencies are significant.

"If we can somehow remove some of the burdens of the technical infrastructure, logistics, and mechanics of conducing clinical trials, it becomes easier to actually ask and answer questions," said Parkinson, who left NCI as head of CTEP in 1997, moving to Novartis and then to Amgen. "That facilitates innovation and it promotes integration of information across the spectrum of trials, facilitating what we all care about, which is knowledge creation."

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Working Group's Recommendations

The working group's report said there is an "urgent need to integrate the successful, but functionally diverse, elements of the current clinical trials system" in order to speed patient accrual to trials, improve the "scientific and bioinformatic infrastructure for clinical studies," and "expand the involvement of all stakeholders in clinical trial development, prioritization, and completion."

In preparing its recommendations, which it said were in "draft" form, the working group opened a Web site for public comment last December. A summary of the comments and the text of the recommendations are available at http://integratedtrials.nci.nih.gov/.

Following is the excerpted text of the recommendations as presented to the NCAB:

Patient Accrual Subcommittee

Goals: Increase the rate of patient accrual to cancer clinical trials. Increase accrual of under-represented segments of the population to clinical trials. Recommendations:

—Provide standardized materials and other resources to help sites plan, staff, implement, and manage clinical trials [by providing] funding for required site personnel, funding for community outreach to recruit a diverse patient population, Web-based trial initiation tools, and educational materials for patients.

—Increase public visibility of NCI programs with the goal of expanding the rate of patient accrual to NCI-sponsored clinical trials. Develop promotional and marketing programs for high-priority studies. Partner with community groups, consumer media and physicians to communicate patient benefits of trial participation. Create tailored programs and community partnerships to engage minorities and special populations.

—Provide incentives that encourage patients and community oncologists to participate in clinical trials. Develop an NCI certification program for clinical oncologists. Educate patients about the unique qualifications of an "NCI-certified investigator." Seek reimbursement for clinical care within qualified clinical trials including counseling, education, etc. Communicate trial results to patients and emphasize their contribution to the care of future patients.

—Improve access to clinical trials for community oncologists and patients. Develop CCOP mentoring programs for interested community oncologists, especially those serving minority populations. Expand use of community-based regional IRBs to decrease lead time and conserve resources. Improve the awareness, functionality and utilization of the CTSU. Create multiple, user-friendly channels, including comprehensive websites, where patients and physicians can find information on cancer clinical trials.

Regulatory Subcommittee

Goals: Enhance cooperation between federal agencies, industry, and other key stakeholders to reduce regulatory burdens and accelerate drug and device development. Develop approaches for increasing the involvement of industry, CMS and other payers in the NCI cancer clinical trials enterprise. Recommendations:

—Develop guidelines/procedures for joint participation of FDA and NCI in meetings, including those with industry, concerning new agents and diagnostics in order to coordinate and accelerate drug and device development.

—Reduce the auditing, monitoring, and regulatory burden on clinical trial sites by coordinating requirements of NCI, FDA, and OHRP in order to identify specific changes that can eliminate redundancy and reduce costs.

—Increase use of the NCI-FDA expedited concept/protocol approval process, including use of the FDA Special Protocol Assessment, for NCI sponsored trials that are intended to impact product labeling.

—In collaboration with CMS and other payers and stakeholders, establish a robust and transparent process for identifying clinical studies that would warrant reimbursement of appropriate clinical trial and investigational costs. These studies would address critical questions about cancer practice faced by patients, clinicians, and other decision makers.

—In collaboration with FDA, ASCO, AACR, and other interested organizations, support training programs designed to increase the number of cancer investigators who are qualified to guide new agents and devices through the development and regulatory process.

Core Research Services Subcommittee

Goals: Enhance access to the scientific infrastructure necessary to facilitate the conduct of high priority correlative science studies to translate new discoveries into clinical practice. Integrate, in an efficient and timely manner, strong scientific review of correlative studies with development and review of clinical protocols. Recommendation:

—Establish annual budgets for studies ancillary to clinical trials, including correlative science, health economics, and quality of life investigations, that can be accessed on a protocol by protocol basis.

Standardization and Infrastructure Subcommittee

Goals: Improve efficiency, reduce duplication of effort, and achieve cost savings. Facilitate innovation and promote integration across trials. Facilitate data interpretation and data comparison across trials. Allow for closer integration of biological measurements and clinical trial findings. Recommendations:

—With concurrence from FDA, establish standards for the essential data to be collected in clinical trials and the format in which it is collected. Define core data elements. Define standardized Case Report Forms. Develop the caBIG standard infrastructure necessary to support clinical trials and interface caBIG with other databases utilizing standard elements. As caBIG is implemented, consolidate redundant systems, where possible.

—Establish a process for official credentialing of research personnel and sites and create a national, central database of credentialed investigators and sites.

—In collaboration with clinical research sites and industry sponsors, establish a set of standard clauses for clinical research contracts that address complex issues such as intellectual property and publication rights.

—Establish a process for development of biomarker standards; set an expectation that correlative science studies will be performed according to standard protocols in credentialed reference labs.

Coordination Subcommittee

Goals: Promote and reward team science and collaborative clinical trial participation. Facilitate information exchange and collaboration among clinical investigators. Enhance the design and planning of new clinical trials by providing investigators with access to comprehensive, up-to-date information about ongoing and completed studies. Enable patients and community oncologists to make better decisions about cancer care by providing access to comprehensive, up-to-date clinical trial information. Recommendations:

—Establish a comprehensive database containing regularly updated descriptive information (protocol, eligibility criteria, sites, accrual, etc.) on all federally funded cancer trials (CTEP, Cancer Centers, SPOREs, P01, R01, etc.), which would be linked to all publicly available information on each trial. Data on adverse events, toxicity, and efficacy would be available to the extramural community as soon as approved for public release. Create a web-based interface to provide investigators with easy access to information for research planning, prioritization and resource allocation. Create additional web-based interfaces to enable other interested parties such as patients to access information.

—Realign NCI funding, academic recognition, and other incentives to promote collaborative team science and the clinical trial cooperation needed to effectively address the most compelling opportunities in cancer research today.

Prioritization Subcommittee

Goals: Provide broad-based scientific and clinical advice to ensure the development and design of the most clinically important and scientifically informative clinical trials. Increase efficient use of resources through an open collaborative process for setting national cancer clinical trial priorities and reducing duplication and overlap. Increase involvement of patients and community oncologists in clinical trial prioritization. Recommendations:

—Establish an external Investigational Drug Working Group to collaborate with NCI staff on strategy, design, and prioritization of drug-specific development plans in early clinical trials for which NCI holds an IND.

—Develop a formal working group mechanism for development and prioritization of disease-oriented phase III trials that leverages the disease intergroup structure, involves the broad oncology community, and facilitates open communication about all relevant studies.

—Enhance involvement of community oncologists and patient advocates in the cancer clinical trials prioritization process through representation on working groups and creation of advisory committees and focus groups.

Working Group-Wide

—Establish a permanent clinical trials subcommittee with broad representation from extramural clinical investigators, community oncologists, regulatory agencies, industry, and patient advocacy groups to advise the NCI director on the conduct, oversight, and implementation of clinical trials across the Institute.

—Develop the necessary organizational structure within the NCI to coordinate the entire clinical trials enterprise supported by the Institute.

Long-Term Goal: Combine the best of all of the components of the NCI-supported clinical trials system to develop a cooperative enterprise built on a stronger scientific infrastructure, and on a broadly-developed and engaged coalition of critical stakeholders who are

essential for the viability of a collaborative national clinical trials research endeavor.

Electronic Case Report Forms: No. 1 Priority

NCAB member Arthur Nienhuis, of St. Jude Children's Research Hospital, noted that many of the recommendations will require additional funds.

"I wondered in thinking about that in a period of time where the budget is flat and we don't anticipate substantial increases, whether there are efficiencies that could be achieved within the current system that potentially would free up the monies to allow you to implement some of these important objectives?" he asked.

Doroshow said bioinformatics could improve efficiency. "I'm not going to stand up here and tell you that those are going to instantaneously provide the dollars to fund all the activities that we need immediately, because it's going to initially cost money to develop that infrastructure," he said.

"If I could do one thing out of all these recommendations that would save the most money and speed the process, it would be to develop an electronic case report form, so that one wouldn't be faced with the task of having 16 different case report forms from 16 different trials that a data manager has to learn," Doroshow said.

NCAB member Carolyn Runowicz said the industry and NCI trials should use standard case report forms.

"The case report forms that overwhelm my office from the different pharmaceutical companies could fill this room, and [we] keep them on file for seven years, and they are all different," said Runowicz, director of the Neag Comprehensive Cancer Center at the University of Connecticut Health Center. "If we could get the FDA to agree to one standardized form--a shorter one, and electronic--that would enhance data management and collection and the speed of trials."

Doroshow agreed. "I don't think it's ever going to be possible to develop a 100 percent of all the elements for everything, because a transplant trial is going to be different from a surgical trial," he said. "But what I think is possible is that 80 percent of the data collected can be agreed upon and the other 20 percent can be what's needed for the specific study. We're going for the 80 percent, which will make an enormous difference."

Steven Averbuch, of Merck Research Laboratories, and co-chairman of the working group's regulatory subcommittee, said industry would "fall into line very rapidly" if FDA were to provide guidelines for standard case report forms.

FDA has no regulations covering case report forms, said Richard Pazdur, director of the FDA Division of Oncology Drug Products and co-chairman of the working group's regulatory subcommittee.

"From a regulatory perspective, this should not be a major issue," he said. "We would be happy to work on this and expedite this, because it's really in the best interests of everyone. We don't construct the case report forms. They are usually coming to us from industry. I could envision… perhaps a core case report form, and then a supplement for each individual protocol that would handle the specifics of that protocol."

Anna Barker, NCI deputy director for advanced technologies and strategic partnerships, said Ken Buetow, director of the NCI Center for Bioinformatics, "is working pretty diligently on this" with FDA. "I think there has been some real progress on this, and I think there will be something coming fairly soon, with an industry working group as well as an academic working group," Barker said.

"Overhaul" of Cooperative Groups?

"There is an enormous redundancy and slowness in the cooperative group mechanism, and a lot of inequities, and I infer from the presentations today that your group would support an overhaul of that mechanism," said NCAB member Runowicz.

Doroshow's answer seemed to indicate that a tune-up, not an overhaul, is in order.

"We did a lot of soul-searching about how do we make what we have better," Doroshow said. "The real issue is that we have such enormous threads that are disconnected, they are not coordinated, and we are spending resources with people who simply don't know what's going on in one area, even within specific disease areas they don't know from one institute to another, from one funding vehicle to another. We need to develop a process that informs the entire specific disease community about what is going on, whether it's a SPORE, a P01, a cooperative group disease committee.

"We need to be not in the politics business, but in the science business," he said. "The science business we can do by informing each other and make sure we are not getting credit for redundancy. That is a critical, critical issue, and that is one of the things we want to address first."

Sponsors don't bring new agents to NCI for development, because the cooperative groups are too slow, said NCAB member Daniel Von Hoff, director of

the Translational Genomics Research Institute.

He said the proposed Investigational Drug Working Group should assign new agents to each cooperative group and push for rapid implementation of trials. "A lot of times it's not the NCI that's the slow part," he said. "Sometimes the investigator is busy, so if [one cooperative group] can't get it done within a three-week period of time, then go on to the next group."

Von Hoff said he also supported the idea of a certifying laboratories where physicians could send patients to have their cancers sequenced for potential targets. "If I had a new diagnostic and it were done in an NCI-certified laboratory, I'd feel a lot better about that," he said. "I'd like every doc in the U.S. to have every person with pancreas cancer to have their tumor sequenced for the EGF receptor mutation. I have no place to go for that."

Barker said that at a conference on biomarkers, sponsored by NCI and FDA and held in Houston earlier this month, participants recommended that NCI bring together the CEOs of diagnostics companies to begin discussions about creating a public database for biomarkers, but companies seemed resistant to that idea.

"So many biomarkers are already lost," Barker said. "Once they are submitted as an IND and the IND is unsuccessful, we never see those biomarkers. The only people who actually know the status of biomarker research is the FDA…. I want to hear from David [Parkinson] and Steven [Averbuch] on how realistic it is to expect us to have participation from the private sector in such a database."

Parkinson said NCI could encourage industry participation.

"The way one changes things is you set the drivers up so that it's either necessary or beneficial for their cooperation," he said. "I think it's inevitable. The new therapeutics we are developing in oncology are all biological probes. It will obviously be public if it's linked with therapeutics development, because it will become part and parcel with the therapeutic. It's public information about the agents.

"My guess is--I wasn't at the Houston meeting--but the pushback probably had to relate to this interface between what is pre-competitive and competitive information," Parkinson said. "That's a transition state in the development of therapeutics. Everything's pre-competitive until it's public. It's public, because it gives you and advantage with the therapeutic, so that's the way to set the drivers up. I don't see this as a long-term problem. It's a transitional problem.

"The fact is, we have not looked at patients with other than a 19th century classification in our therapeutics development," Parkinson said. "It's time to change it. Associated with that change is a whole reconfiguration of our conceptualization of cancer…. We shouldn't be developing agents for colon cancer. We should be developing agents for pathophysiological states which require some characterizations. I don't see this as a long-term problem at all. It will be just a reconfiguration of what our concept of what cancer is."

FDA's Pazdur said the agency encourages sponsors to submit data on biomarkers.

"What we know about biomarkers is only what companies submit, and, therefore, we are, through a series of guidances, trying to encourage the sponsors to submit data to us that will not be held against them," he said. "We have a guidance on this that establishes what is a known biomarker, what's an exploratory biomarker, to try to get this data into the FDA and have a dialogue with the companies, without a fear of retribution."

Richard Schilsky, associate dean for clinical research in the Biological Sciences Division at University of Chicago, chairman of Cancer and Leukemia Group B, and chairman of the working group's patient accrual subcommittee, agreed with Von Hoff's suggestion for certifying labs.

"If we are trying to do a broad-based national clinical trial that is evaluating a targeted agent or a molecular diagnostic, we have enormous difficulty right now in actually finding standard reference laboratories that can serve as the reference lab for a study that may involve thousands of patients, so that we can ultimately get reliable data," Schilsky said. "So we need a mechanism to develop, certify, and then utilize standard reference laboratories for a range of different biomarkers that might be evaluated in clinical trials."

Once biomarkers become clinically useful, "we also need minimum standards for the way those biomarkers are deployed in the marketplace," Schilsky said. "We have to have some level of confidence that if there are a thousand labs doing that, we are going to get similar results."

NCAB member Jean deKernion, chairman of urology at the School of Medicine at University of California, Los Angeles, said researchers often can't get enough drug for studies. "We have insufficient resources to produce biologic-grade material for a number of the translational projects that are sponsored by the NCI," he said. "I don't know if it fits into the future of the committees that we are talking about, but it's something we have to pay a lot of attention to."

NCI "Prepared To Make Changes"

The report gives NCI an "overarching functional design" for the clinical trials system, von Eschenbach said to the NCAB.

"We need more specificity now with regard to the architectural plans and the timelines for the staging and coordination of building this new construct," he said. "I am prepared to make the structural changes that have to be made. I'm prepared to make the functional changes that have to be made…. It must get done if we are going to fulfill the [NCI] mission and the goal of [eliminating suffering and death due to cancer by] 2015.

"I am absolutely confident that at the end of the day very, very soon, we will see in place in this country a clinical cancer research enterprise that will be effective and efficient, adapted to the new reality of not simply targeted, mechanistic-based drugs, but the fact that we're not developing just drugs, we're truly developing therapies. This system will have to adapt to the fact that in many of these cases, it will be the integration and combination of not just drugs, but biologics, and even the diagnostic and monitoring devices associated with imaging and profiling. So we have an exciting opportunity and an exciting future.

"This committee has set the stage. It has put in place what I believe is an absolutely phenomenal plan and opportunity for us to create what we all have been longing for and wanting and waiting for, but never seeming able to get. This committee has gotten it all together."

Funding Opportunities:

Program Announcement

PAR-05-042: Specialized Programs of Research Excellence in Human Cancer for Year 2005-2006

Letters of Intent Receipt Date: March 23 for lung and genitourinary cancer (bladder, kidney, testicular, not prostate); July 23 for skin and prostate cancer.

Application Receipt Dates: May 23 for lung and genitourinary; Sept. 23 for skin and prostate.

NCI Organ Systems Branch invites grant applications for SPOREs in organ-specific cancers. Applicant institutions are to demonstrate their ability to conduct translational research in prevention, etiology, screening, diagnosis, and treatment of lung, genitourinary, prostate, or skin cancers. Required components of a SPORE include: a minimum of four translational research projects, cores, developmental research and career development programs. A required core in a SPORE is a human cancer tissue core for the particular organ-site that will benefit translational research. The support for SPOREs is through an NIH specialized center grant P50 mechanism. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PAR-05-042.html.

NCI has revised the SPORE Guidelines, available at http://spores.nci.nih.gov.

Inquiries: Jane Fountain, (Skin Cancer SPOREs) e-mail: jf227t@nih.gov; Peter Ujhazy, (Lung Cancer SPOREs) e-mail pu5s@nih.gov; Andrew Hruszkewycz (Genitourinary and Prostate Cancer SPOREs) e-mail ah5x@nih.gov; Organ Systems Branch phone 301 496-8528; fax 301-402-5319.

RFP Available

RFP N01-CP-51010-66: Continuation of Follow-up of DES-Exposed Cohorts

Response Due Date: April 4

NCI Division of Cancer Epidemiology and Genetics, Epidemiology and Biostatistics Program, is seeking collaborative investigators to continue follow-up of established DES cohorts to measure the incidence and mortality of cancer, especially cancers of the breast and reproductive system. The secondary objectives include assessment of other health effects suggested as being related to DES exposure, monitoring for as yet unanticipated health risks, and utilization of the cohorts as a platform to launch more intensive and focused case-control studies of specific DES-related conditions. Each collaborating investigator shall be required to furnish all the necessary services, qualified personnel, material, equipment, and facilities, not otherwise provided by the government, as needed to continue follow-up of surviving members of a cohort of at least 500 women and men exposed to diethylstilbestrol in utero. Disease outcomes will be ascertained by means of questionnaires, medical record review, and tissue sampling as appropriate. The contracts to be awarded will be cost-reimbursement, completion types.

The RFP is available at http://www.fbodaily.com/archive/2005/02-February/04-Feb-2005/FBO-00744308.htm.

RFA Available

RFA-AI-05-002: Units for HIV/AIDS Clinical Trials Networks

Letters of Intent Receipt Date: June 10

Application Receipt Dates: July 11

The RFA solicits applications for CTUs to implement the clinical research plans of one or more of the HIV/AIDS Clinical Trials Networks. Each CTU will be led by a principal investigator, comprised of an administrative component and one or more clinical research sites, and configured to conduct clinical research by recruiting, screening, enrolling and following research participants from the populations most affected and/or endangered by the HIV/AIDS epidemic. The AIDS Malignancy Consortium (URL: http://www.amc.uab.edu) is an NCI-supported clinical trials group, founded in 1995 to conduct trials for AIDS-associated malignancies. The NCI will likely recompete the AMC in a timeframe that overlaps this competition. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-05-002.html.

Inquiries: For NCI--Jodi Black, Division of Cancer

In Brief:

Holland To Receive Burchenal Award At AACR Meeting

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Feb. 3 in Paris. Holland, the founder of the field of psycho-oncology, will receive the Joseph Burchenal Prize at the American Association for Cancer Research annual meeting April 20. She is the former chairman of the Department of Psychiatry and Behavioral Sciences, Memorial Sloan-Kettering Cancer Center. . . . **ROBERT WEINBERG** received the Raymond Borguine Award for Cancer Science at the International Congress of Anti-Cancer Treatment. He is the Daniel K. Ludwig and American Cancer Society Professor for Cancer Research at Massachusetts Institute of Technology. . . . **NCI DIRECTOR'S** Consumer Liaison Group opened a Web site to increase the Institute's communication with cancer advocates and the public: http://ncilistens.cancer.gov. The site "will allow NCI to solicit opinions on important topics," said DCLG Chairman **Douglas Ulman**, director of survivorship at the Lance Armstrong Foundation. "DCLG will monitor the process, reviewing all of the comments and alerting NCI to important themes and issues of concern to the broad cancer advocacy community and the general public." NCI and DCLG will pose questions and discussion topics on a monthly basis. Advocacy groups would need to register on the Web site and designate a representative to submit comments on the organization's behalf. NCI will summarize comments and post a response. . . . **REPORT ON CARCINOGENS**, Eleventh Edition, was released by the National Toxicology Program. The report adds 17 substances to the list of cancer-causing agents, bringing the total to 246. For the first time, viruses are listed: hepatitis B, hepatitis C, and human papillomaviruses. Other new listings include lead and lead compounds, X-rays, compounds found in grilled meats, and substances used in textile dyes, paints and inks. The report is available at http://ntp.niehs.nih.gov. . . . **HHS** has a new mechanism for research institutions that receive HHS funding to obtain an assurance of compliance with regulations for the protection of human subjects. A single Web-based "Federalwide Assurance" will replace several types of assurances. The new process will reduce the burden of compliance, said **Bernard Schwetz**, director of the Office Human Research Protection. Institutions will have 11 months to transition to the new system. Further information: www.hhs.gov/ohrp/assurances/assurances_index.html.

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THE CANCER LETTER

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Business & Regulatory Report

Product Approvals & Applications:

FDA Approves Doxil For Ovarian Cancer; Label Updated With Phase III Trial Data

Tibotec Therapeutics, a division of Ortho Biotech Products, L.P., of Bridgewater, N.J., said FDA has granted approval to Doxil (doxorubicin HCl liposome injection) for ovarian cancer where disease has progressed or recurred after platinum-based chemotherapy.

The label for the drug has been updated to include survival, time to disease progression and tumor response rate data from a randomized phase III study, the company said.

"The phase III data provide evidence of the clinical benefit for patients

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Deals & Collaborations:

Univ. of Pittsburgh, ZelleRx, To Develop ZRX101 For Melanoma, Other Cancers

University of Pittsburgh Medical Center said it would provide services valued at more than $1 million to **ZelleRx Corp**. to develop cancer treatment candidates based on its proprietary natural-killer cell line, in exchange for equity in the company.

The services will include support of phase I and phase II trials for ZRx101, the ZelleRx cancer treatment, the company said. The treatment was developed using the ZelleRx proprietary natural-killer cell line, NK-92. The trials will focus first on melanoma, the company said.

To date, 25 patients have been treated with the drug for renal and melanoma cancers in Chicago, and advanced cancers in young adults (leukemia and sarcomas) in Frankfurt, Germany, the company said.

NK cells are the first cells of the defense system that identify and destroy cancer tumors and other infected cells, the company said. Ronald Herberman, who, after leaving NIH in 1985, joined the UPCI as its founding director, first identified the cells in the early 1970s at NIH.

"It is exciting for the University of Pittsburgh Cancer Institute to play a leading role in exploring the therapeutic effects of this very potent, standardized NK cell therapy, which I believe has great potential to benefit patients with various types of cancer," said Herberman.

* * *

Asterand Inc of Detroit said it would distribute 11 breast cancer cell lines, known as SUM, from the **University of Michigan** for research processes. The cell lines can be used to study all aspects of breast cancer biology, from drug target identification to cell signaling to effects of novel

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Doxil Label Is Updated With Phase III Trial Data

(Continued from page 1)

with relapsed ovarian cancer," said Alan Gordon, of the University of Arizona School of Medicine and Arizona Gynecologic Oncology, and lead author of the study, known as Doxil Study 30-49.

In the randomized, multi-center, open-label study, 474 patients with recurrent epithelial ovarian cancer were assigned to receive either Doxil 50 mg/m^2 every 28 days or topotecan HCl 1.5 mg/m^2/day for five consecutive days every 21 days, the company said. In the trial, 239 patients received Doxil; 235 received topotecan HCl.

The primary endpoint, time to disease progression after starting therapy, was comparable for the two groups. The median time to disease progression was 4.1 months for the Doxil group and 4.2 months for the topotecan HCl group; the p value, a statistical measurement, was 0.617.

The overall median survival was 14.4 months for patients treated with Doxil and 13.7 months for patients treated with topotecan HCl; the p value was 0.05. The p value was not adjusted for multiple comparisons. The overall tumor response rate for Doxil-treated patients was 19.7 percent and 17 percent for topotecan-treated patients, the company said.

Because myocardial damage could lead to congestive heart failure and might be encountered as the total cumulative dose of doxorubicin HCl approaches 550 mg/m^2, Doxil could lead to cardiotoxicity, the company said. Therefore, Doxil should be administered to patients with a history of cardiovascular disease only when the benefit outweighs the risk, the company said.

Acute infusion-associated reactions have occurred in up to 10 percent of patients, the company said. Serious and sometimes life-threatening or fatal allergic/anaphylactoid-like infusion reactions have been reported. Medications to treat such reactions, as well as emergency equipment, should be available for immediate use. Severe myelosuppression may occur.

In clinical studies in recurrent ovarian cancer, the most common side effects reported with Doxil therapy included hand-foot syndrome, nausea, mouth sores, tiredness, abdominal pain, vomiting, constipation, rash, fever, reduced red blood cell count, reduced white blood cell count, weakness, hair loss, appetite loss and diarrhea, the company said. Some patients experienced infusion-related reactions and skin reactions.

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Advanced Life Sciences, of Woodridge, Ill., said its compound ALS-357 for malignant melanoma has been granted an IND license.

The company said it would evaluate the safety and tolerability of the topical application in clinical trials for transit metastatic disease involving the skin.

ALS-357, a natural product derived from birch bark, has demonstrated anti-tumor activity against malignant melanoma, the company said.

* * *

BioGenex Laboratories Inc. of San Ramon, Calif., said it has received FDA pre-market approval for its InSite Her-2/neu Kit, which identifies breast cancer patients eligible for treatment with Herceptin (trastuzumab).

InSite Her-2/neu is a complete kit, in manual and automated format, containing all components for the performance of immunohistochemistry staining of breast cancer tissue. The automated format is approved for use on the BioGenex i6000 Automated Staining System and the OptiMax Plus Consolidated Staining System. Both manual and automated versions of the kit will be marketed worldwide.

The test detects a protein (Her-2/neu tyrosine kinase) that stimulates cancerous cell growth, the company said. Overexpression of the Her-2/neu protein is seen in 25-30 percent of breast cancer patients. The detection of the protein indicates eligibility for breast cancer treatment with drug Herceptin, developed and

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marketed by Genentech.

BioGenex said it would seek FDA approval to use the automated format of the InSite Her-2/neu Kit on its new system. The system is designed to automate all of the assay steps required to perform IHC, In Situ Hybridization and Fluorescence In Situ Hybridization, including the application of coverslip, resulting in a completely finished slide that is ready to go directly on the microscope for review.

Last October, BioGenex has entered into an agreement with Abbott to develop automated solutions using the system for the Abbott FISH-based tests, the company said. BioGenex said it has granted Abbott distribution rights for marketing the new system worldwide in the FISH diagnostics field.

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Debiopharm S.A of Lausanne, Switzerland, said **Sanofi-Aventis** has received FDA marketing approval for a new formulation of Eloxatin (oxaliplatin for injection).

The formulation, available in two different presentations of 50mg and 100mg, is a clear, preservative-free, ready for use solution, the company said.

The injection used in combination with infusional 5-FU/LV, is indicated for adjuvant stage III colon cancer where a complete resection of the primary tumor has occurred, and for advanced carcinoma of the colon or rectum, the company said.

Initiated by Debiopharm after the approval of the lyophilised formulation of Eloxatin, the aqueous solution was then jointly developed with Sanofi-Aventis, which is marketing the formulation in over 60 countries, Debiopharm said.

* * *

Envisioneering Medical Technologies of St. Louis said FDA approved its device for prostate biopsies and improving the accuracy of less-invasive cancer treatments

The device, TargetScan, is an innovation in prostate mapping, biopsy and cancer treatment guidance, the company said. Combining 3-D image acquisition with a stationary probe, this new technology helps plan and execute targeted prostate biopsies--potentially improving patients' cancer treatment outcomes with less-invasive procedures.

Current procedures require urologists to hold and pivot a probe with one hand, while performing a needle biopsy with the other hand. The inherent variables of this existing biopsy technique can force doctors to miss as much as 20 to 30 percent of potential cancers, said Gerald Andriole, professor of surgery and chief of urology at Washington University School of Medicine and director of the Urological Research Center at Barnes-Jewish Hospital in St. Louis.

"We've learned that current diagnostic tools are inadequate—missing cancer in some patients while over testing others," said Andriole, a member of the Envisioneering medical advisory board.

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Implant Sciences Corp. (AMEX: IMX, IMX.WS) said it received approval of its 510(k) premarket notification from FDA for Ytterbium-169 radioactive source for breast and other cancers.

The company said it would take the following steps in the next six months to commercialize its product: register the radioactive source by the Massachusetts Radiation Control Program and receipt of a National Institute of Standards and Technology traceable calibration. In addition, the company said it would supply the radiation source to radiation oncologists for a pilot clinical evaluation of the radioactive source.

Many patients decline breast conserving lumpectomy because of the time and travel burdens imposed by six to seven weeks of traditional external beam radiation therapy, the company said. Ytterbium-169 source for APBI is administered on the tip of a wire into a lumpectomy cavity for 8 to 10 short (15 minute) periods over 4 to 5 days, the company said. In addition, the source will be sold in conjunction with a portable shielding apparatus developed by Implant Sciences, which is patent pending.

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Johnson & Johnson Pharmaceutical Research & Development, L.L.C. of Raritan, N.J., said it has completed the submission of an NDA for tipifarnib, an investigational cancer drug, to the FDA Continuous Marketing Application Pilot-1 Program.

Tipifarnib, administered orally, is being investigated in patients 65 years of age and older with newly diagnosed acute myeloid leukemia, the company said.

Under the CMA Pilot-1 Program, J&JPRD said it submitted reviewable units of the tipifarnib NDA as they were completed, receiving ongoing feedback from FDA. The standard FDA review time for the CMA Pilot-1 Program is six months following submission of the final reviewable unit, the company said. Tipifarnib also was granted orphan drug status.

In addition to funding global clinical studies for tipifarnib, J&JPRD collaborated with the NCI Cancer Therapy Evaluation Program, the company said. CTEP, under a clinical trials agreement between J&JPRD and NCI, conducted the phase II study that supports the

tipifarnib NDA.

In October 2004, J&JPRD said it initiated the phase III international study and continues to investigate other uses of the treatment in solid and hematologic malignancies, including stages of myeloid leukemia.

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Norwood Abbey Ltd. (OTC: NABYF) (ASX: NAL) of Melbourne, Australia, and **TAP Pharmaceutical Products Inc**. of Lake Forest, IL, said FDA has accepted their NDA for a bone marrow transplant treatment.

Richard Champlin, of M.D. Anderson Cancer Center, will be the principal investigator, the company said. A consortium of clinicians and institutions will also be involved, including the Dana-Farber Cancer Institute and the University of Minnesota. The consortium is led by Lee Nadler, of the Dana-Farber Cancer Institute Harvard Medical School and is co-funded by NCI and National Institute of Allergy and Infectious Diseases, the company said.

The endpoints will be the determination of immune responses to four vaccines, as an indicator of improved immune function in patients undergoing an autologous BMT, the company said. The phase II, double-blind placebo controlled study will begin within the next three months.

A second BMT trial (NIM-LETR-03) for allogeneic BMT would begin once the autologous trial is initiated, the company said.

* * *

Osiris Therapeutics Inc. of Baltimore said it has received Fast Track designation from FDA for Prochymal, an adult stem cell product formulated for acute graft vs. host disease.

Prochymal, now entering phase II trials, is a formulation of a specific type of adult stem cell that has the ability to modulate the immune system, the company said. Osiris said it has already successfully completed a two-year phase I study.

* * *

R2 Technology Inc. of Sunnyvale, Calif., said it has received FDA approval to expand the use of its ImageChecker D product for CAD system for use with the Siemens Medical Solutions (NYSE: SI) MAMMOMAT NovationDR and viewed on the Siemens MammoReportPlus softcopy reporting workstation.

Under an agreement signed in 2002 and renewed in 2005, Siemens and R2 have exclusive worldwide distribution rights to sell the R2 customized product in combination with Siemens MAMMOMAT NovationDR, the companies said.

"Siemens Medical teamed up with R2 Technology in 2002 to customize and develop innovative technology to promote women's healthcare and the early detection of breast cancer worldwide," said Holger Schmidt, head of the special systems division at Siemens Medical Solutions.

By combining our excellent products, we have created innovative solutions that improve our customer's workflow and their quality outcome,"

Computer-aided detection is used when reading mammograms, the company said. Clinical trials demonstrated that using the R2 ImageChecker system could result in earlier detection of up to 23.4 percent of the cancers detected with screening mammography in women who had a prior screening mammogram 9-24 months earlier, the company said.

* * *

Sonus Pharmaceuticals Inc. (Nasdaq: SNUS) of Bothell, Wash., said it has been granted an FDA orphan drug designation for Tocosol Paclitaxel for non-superficial urothelial cancer.

The designation adds to the Fast-Track designation awarded in 2003 by the FDA Division of Oncology Drug Products to develop the product for metastatic or locally advanced, inoperable transitional cell carcinoma of the urothelium, the company said.

Tocosol Paclitaxel is a novel formulation of paclitaxel, for solid tumors, the company said.

Sonus said it also is pursuing market entry through a 505(b)(2) NDA for an indication for which paclitaxel-based products have already been approved, e.g. breast, ovarian or lung cancers.

The company said it is conducting phase IIb bladder cancer studies in Cleveland, Philadelphia, Baltimore and Seattle, and will soon be opening sites in Spain and the U.K. In addition to the bladder cancer program, Sonus is also conducting a phase IIb study of the treatment for metastatic breast cancer.

Sonus said it has completed enrollment in phase IIa studies of the product for bladder, ovarian and lung cancer patients, the company said. The trials have demonstrated encouraging data on safety and anti-tumor activity, the company said.

Tocosol Paclitaxel is a ready-to-use formulation, which does not require reconstitution, dilution or pharmacy preparation as is required with the marketed paclitaxel products, the company said. Additionally, Tocosol Paclitaxel is administered to patients in a short 15-minute infusion, compared to the three-hour infusion required with Taxol, the innovator paclitaxel product.

* * *

Zila Inc. (Nasdaq: Zila) of Phoenix said FDA has

given marketing approval to the Zila tolonium chloride product as an adjunct to a ViziLite examination for oral cancer.

The oral examination system would evaluate oral muscosal lesions, the company said. ViziLite identifies lesions using chemiluminescent light and then swabs containing ZTC are used to mark the lesions for further examination.

The multi-center clinical study to support the FDA market clearance was conducted in the oral medicine centers at the University of California at San Francisco, the University of Illinois at Chicago and the University of British Columbia, the company said.

Deals & Collaborations:

Asterand To Distribute SUM Cell Lines From Ethier Lab

(Continued from page 1)

drugs on cellular proliferation.

The SUM cell lines, derived in the laboratory of Stephen Ethier, of the Karmanos Cancer Institute, are among the most well characterized cancer cell lines, the company said.

Each cell line, derived from a single patient, represents a different subtype of breast cancer, the company said. All of the known oncogenes with altered expression patterns in breast cancer, in various combinations, are represented and characterized in the SUM lines. In addition, the lines were isolated and grown under defined conditions. Isolation and growth conditions, along with gene expression data through the use of Affymetrix GeneChips, biomolecular markers, such as estrogen receptor and Her2 status, as well as the knowledge in over 50 publications in peer reviewed journals, is available to scientists purchasing the cell lines.

In addition to providing the cell lines, Asterand said it would curate all the molecular information associated with the cell lines. Treatment effects, high-throughput screening, time course studies and functional assays are tractable by using human cell lines.

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CeMines Inc. of Golden, Colo., and **Children's Hospital** of Denver entered into a joint clinical research project in childhood leukemia.

The project, sponsored by CeMines, is based on the CeMines Molecular FingerPrinting, a minimally invasive diagnostic process, the company said.

The research will be conducted by Toomas Neuman, chief scientific officer of CeMines, and by Nicholas Foreman, Tanner Seebaum, associate professor of pediatrics, and Zachary Tschetter, chairman in neuro-oncology, and director, Pediatric Neuro-Oncology Program, at The Children's Hospital-Denver.

"Our project analyzes messenger RNA anomalies from pediatric patients who have been diagnosed with childhood leukemia," said Neuman. "We are able to detect changes of blood-based cancer cells in minute quantities. Our research with Dr. Foreman is important, because it will be the very first demonstration of our CeMines Molecular FingerPrinting technology for a blood-based cancer, such as childhood leukemia," he said.

* * *

Curis Inc. (Nasdaq: CRIS) of Cambridge, Mass., said it has elected to exercise a co-development option with partner, **Genentech Inc**. (NYSE: DNA), and will now share in U.S. development costs and future net profits of a therapeutic product candidate for the topical treatment of basal cell carcinoma.

"We believe that co-development may provide a means of managing the risk of clinical development while at the same time allowing us to retain greater upside potential on certain promising programs," said Daniel Passeri, president and CEO of Curis.

Curis said it would file an IND with Genentech so that clinical investigation of the product candidate could begin.

The collaboration agreement with Genentech established the continued development of a set of anti-cancer technologies based on inhibition of the Hedgehog signaling pathway, including small molecule Hedgehog pathway inhibitors, the company said.

Under the collaboration, Curis retains a co-development option to share in costs and future net profits, specifically for one of the small molecule Hedgehog pathway inhibitors, the company said. The co-development right applies solely to the U.S. marketplace and includes applications for basal cell carcinoma and any additional indications for which this product candidate may be developed.

By exercising the co-development and equal cost-sharing option, Curis said it would incur $20 million in development expenses through phase II trials, a portion of which will be booked in the first quarter of 2005. Curis said it would incur additional costs to complete phase III trials and complete the regulatory approval process. In exchange for the investment, the company said it has increased its downstream revenue potential, through its right to a commensurate share in U.S. net profits.

In addition to the U.S. market, Curis said it would

receive milestone payments and a royalty on any international sales of the topical Hedgehog antagonist.

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Morphotek Inc. of Exton, Pa., said it has been awarded a developmental project grant from the Network for Translational Research in Optical Imaging Consortium of NCI for antibody research with enhanced antibody dependent cellular cytotoxicity activity from genetically evolved cell lines generated using the Morphotek proprietary Morphodoma technology.

The program would generate in vitro and in vivo high throughput assays to screen and identify genetically optimized antibody-producing cell clones yielding antibodies with enhanced ADCC as compared with that of the parental antibody for therapeutic development, the company said.

Morphotek said its Morphodoma platform process optimizes antibody-producing cell lines to yield subclones producing antibodies with higher affinity, enhanced ADCC or cells with enhanced titers for scaleable manufacturing. Cells are optimized via whole genome evolution using Morphodoma technology yielding pools of evolved sibs exhibiting target characteristics. The grant supports novel research utilizing high throughput assays to rapidly detect ADCC activity of antibodies in vitro and in vivo.

* * *

Prolexys Pharmaceuticals Inc. of Salt Lake City signed an exclusive licensing agreement with the Massachusetts Institute of Technology, acting as licensing agent for the Whitehead Institute for Biomedical Research of Cambridge, MA and Columbia University of New York City.

The agreement provides Prolexys, a privately held company, with exclusive, worldwide rights to a patent estate covering selective anti-tumor compounds discovered by Brent Stockwell, a former Whitehead Fellow, now an assistant professor of Biological Sciences and Chemistry at Columbia University.

Additional intellectual property was developed by Stockwell and scientists at Prolexys as part of a joint research collaboration initiated in December, 2003. The licensed compound series are small molecules with unique cancer specific cytotoxic properties that act via a novel mechanism discovered at Prolexys using its chemiproteomics technology.

"The critical groundwork laid by Dr. Stockwell has enabled a very productive and successful collaboration between our two groups," said Sudhir Sahasrabudhe, chief scientific officer of Prolexys Pharmaceuticals. "Working together, we rapidly characterized the compound's novel mechanism for producing cancer specific cytotoxicity and are excited about the development path forward toward the clinic."

* * *

Proxima Therapeutics Inc., of Alpharetta, Ga., said it has entered into a definitive agreement to be acquired by **Cytyc Corp.** (Nasdaq: CYTC).

Under the agreement, the acquisition will be an all cash transaction of $160 million plus a two-year earnout based on incremental sales growth in 2005 and 2006, the company said.

The MammoSite Radiation Therapy System, the Proxima leading product, allows for partial breast irradiation after lumpectomy, the company said. The device is a balloon catheter that delivers a prescribed dose of radiation from inside the cavity created by the removal of the breast tumor in just five days.

Since its clearance by FDA in 2002, MammoSite has been used to treat more than 7,000 breast cancer patients, the company said. In addition to MammoSite, Proxima markets the GliaSite RTS, a site-specific radiation treatment for brain tumors.

* * *

Seattle Genetics Inc. (Nasdaq: SGEN) of Bothel, Wash., said **CuraGen Corp**. (Nasdaq: CRGN) has exercised its option to designate a second antigen target under the existing antibody-drug conjugate collaboration, triggering a $1 million payment to Seattle Genetics.

SG said it entered into the ADC collaboration with CuraGen in June 2004, at which time CuraGen paid an upfront fee of $2 million for access to the ADC technology for one antigen target.

"ADCs are becoming an increasingly important aspect of antibody-based therapy development because the cytotoxic payloads they deliver and release within target cells can enhance the therapeutic potential of antibodies that have targeting ability but lack sufficient potency on their own," said Clay Siegall, president and CEO of Seattle Genetics.

Under the agreement, CuraGen has rights to use the Seattle Genetics ADC technology with antibodies against up to two targets selected by CuraGen, the companies said. CuraGen said it would also pay ongoing technology access and material supply fees and make progress-dependent milestone payments and pay royalties on net sales of ADC products. CuraGen is responsible for research, product development, manufacturing and commercialization of any products resulting from the collaboration.

The SG ADC technology utilizes the targeting

ability of monoclonal antibodies to deliver cell-killing payloads to specific cells, the company said. The technology employs synthetic drugs that can be attached to antibodies through proprietary linker systems. The linkers are designed to be stable in the bloodstream but to release the drug payload under specific conditions once inside target cells, thereby sparing non-target cells many of the toxic effects of traditional chemotherapy.

By linking drug payloads to monoclonal antibodies, ADCs can increase the therapeutic potential of antibodies that have inherent cell targeting ability but lack sufficient cell-killing activity, the company said.

* * *

Serologicals Corp. (Nasdaq: SERO) of Atlanta said **Chemicon International Inc.** of Temecula, Calif., its wholly owned subsidiary, has acquired the assets of **Specialty Media**, of Phillipsburg, N.J., for $6.5 million in cash, thereby expanding its stem cell franchise.

"The transaction, which we expect to be immediately accretive, will provide us an expanded platform on which to continue to add new stem cell product opportunities for the stem cell research market," said Jeffrey Linton, president of Chemicon International "We expect to generate approximately $4 million from the sale of Specialty Media's products in 2005."

The acquisition gives Chemicon additions including the following: products and manufacturing capabilities for stem cell lines and support reagents such as feeder cells and media; enzyme-free, animal-free, chemically defined cell dissociation solutions and cell freezing media, qualified for stem cell culture; basal and complete cell culture media, custom formulations, solutions and powders; and stem cell qualified supplements including antibiotic solutions, the company said.

The products join the Chemicon stem cell product portfolio that includes stem cell differentiation and characterization kits, a line of stem cell marker antibodies, and ready-to-use stem cell media and stem cell culture supplements such as ESGRO and Leukemia Inhibitory Factor, an exclusively licensed growth factor for the derivation and maintenance of mouse ES cells, the company said. Recent additions to the Chemicon stem cell tools include RESGRO, an ES cell culture medium for the rescue of partially differentiated ES cells as well as the derivation of new ES cells, and the PluriStem mouse ES cell-lines.

Specialty Media is a division of Cell & Molecular Technologies and owned by Sentigen Holding Corp. (Nasdaq: SGHL).

* * *

University of Cambridge, **Cancer Research Technology**, **Cancer Research UK** and **Perlegen Sciences Inc.** (Nasdaq: AFFX) of Mountain View, Calif., said they would conduct a high-resolution, whole genome association study for breast cancer.

Over 200 million individual genotypes in DNA samples would be collected to reveal the genetic basis of the disease, the companies said.

Results will be validated by analysis of thousands of additional samples coordinated by the researchers at University of Cambridge through clinical collaborators, the companies said. The search would identify women at high risk and lead to improvements in the prevention, earlier detection and treatment.

Cancer Research UK said it is providing funding for the research.

The study will be a genome-wide scan for common predisposing genetic variants that are associated with susceptibility to breast cancer, the companies said.

DNA samples were collected through a systematic study of breast cancer in the Anglian region of the UK and through clinical genetics centers in the UK, the companies said. Genetic variants in the DNA of breast cancer cases would be compared with DNA from healthy women in the European Prospective Investigation of Cancer study of diet and cancer also coordinated at Cambridge. Perlegen Sciences said it would genotype the anonymized samples to determine the genetic variation in each sample.

Clinical Trials:

Aphton Says Phase III Trial Didn't Meet Primary Endpoint

Aphton Corp. (Nasdaq: APHT) said its phase III study of Insegia (G17DT immunogen) in combination with chemotherapy didn't meet its primary efficacy endpoint of improving overall survival in pancreatic cancer.

Insegia is an immunotherapy directed at the growth hormone gastrin, the company said. The study randomized 383 untreated patients with metastatic pancreatic cancer to receive Insegia plus Gemzar (gemcitabine) versus gemcitabine alone.

The adverse event profile showed no significant differences between study arms and was similar to the observed events in previous clinical trials, the company said.

"While Insegia did not meet the primary endpoint, we are encouraged by results we have observed in patients who achieved an antibody response, in this case approximately 70 percent of patients," said Patrick

Mooney, CEO of Aphton. "The patients demonstrated prolonged survival over patients treated in the control arm with chemotherapy alone, as well as over patients who did not achieve an antibody response. We also believe that the results further support the current monotherapy applications of the therapy as a treatment where chemotherapy is not an option."

In May, Aphton reported positive data from a phase II combination therapy trial with cisplatin and 5-Flourouracil in advanced gastric cancer. In addition to the combination studies for the drug, Aphton said it has also completed and reported positive data from a phase III monotherapy pancreatic cancer trial, for which it has filed for marketing approval in Canada, Australia and Switzerland.

* * *

Perlegen Sciences Inc. of Mountain View, Calif., said it has been awarded a grant from NCI to study tumor-specific DNA mutations involved in colorectal cancer in collaboration with the Sidney Kimmel Comprehensive Cancer Center at **Johns Hopkins University**.

The research could lead to a better understanding of the disease, improved tools for cancer detection and diagnosis, new targets for therapeutic and preventive intervention, and opportunities for more individualized treatment, the company said.

In an effort to identify and characterize cancer genes, the team will analyze at single-base resolution the DNA sequences of thousands of genes in colorectal tumor tissue as well as in normal tissue from the same patients. This effort is expected to lead to the identification of a significant number of tumor-specific mutations, providing insight into the cause of disease.

* * *

SpectRx Inc. (OTCBB: SPRX) of Atlanta said it is collaborating with **Emory University** as part of a grant to Emory from the **Georgia Research Alliance** to support clinical trials for a non-invasive cervical cancer detection device.

The $64,700 matching grant will be used for the clinical trial of the SpectRx-developed technology at Grady Memorial Hospital under the guidance of Lisa Flowers, of Emory University, the company said.

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

A clinical study of the technology, sponsored by NCI, indicated that the non-invasive test could reduce by 55 percent the number of unnecessary follow-up procedures as a result of false positive Pap test results, the company said.

Oncology Management:

Salick Health Care Changes Name To Aptium Oncology

Salick Health Care of Los Angeles changed its name to **Aptium Oncology**.

Founded over 20 years ago, the company designed, built and managed cancer centers at hospitals including Cedars-Sinai Medical Center, Mount Sinai Medical Center, New York University and Alta Bates Summit Medical Center.

The company was founded by physician entrepreneur Bernard Salick and is now a unit of AstraZeneca.

"As the company embarks on a new growth phase, we are taking the opportunity to introduce an updated vision that builds upon our core competencies in oncology, while conveying a message that is compelling and relevant in today's healthcare marketplace," said Peter Jessup, chief executive officer and president of Aptium Oncology. "We selected the name 'Aptium Oncology' because we believe it is well-suited to both of these efforts."

Aptium's goals include the creation of a national network of managed cancer centers that afford hospitals and physicians the advantages of expert clinical, technical and administrative resources.

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i3Archive Inc. of Philadelphia announced the on-line availability of its National Digital Mammography Archive to women directly.

The company's Patient Portability Program now provides access to the NDMA resources as well as to a private, HIPAA compliant web portal, where a patient can record and retrieve her own personal healthcare information. "Using IBM grid technology, the National Digital Mammography Archive allows for quick retrieval of mammography images from a central archive," said Mike Svinte, Vice President, Information Based Medicine EBO, IBM.