THE CANCER LETTER INTERACTIVE

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Congressional Committee, SEC Probe ImClone's Statements To Shareholders

A Congressional committee last week began an investigation of ImClone Systems Inc. In letters dated Jan. 18, the House Committee on Energy and Commerce and its subcommittee on Oversight and Investigation asked FDA, ImClone, and its partner Bristol-Myers Squibb to provide documents related to clinical trials of C225.

Separately, the Securities and Exchange Commission began an "informal inquiry" of the New York-based biotechnology company. According to a letter by SEC officials, the agency is probing "possible

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In Brief:

Venter Steps Down As Celera President; Moffitt, Puerto Rico Center Win NCI P20 Grant

J. CRAIG VENTER has stepped down as president of the Celera Genomics Group of Rockville, MD, although he will continue as chairman of the Celera scientific advisory board. **Tony White**, chairman and CEO of Applera, the parent company, will assume the presidency of Celera on a temporary basis. "We are now at a critical juncture where my best contributions can be made in a scientific advisory role, allowing the rest of the organization to continue Celera's progress toward becoming a successful pharmaceutical business," Venter said. "I also intend to spend more time fulfilling my role as Chairman of the Board of The Institute for Genomic Research." . . . **H. LEE MOFFITT** Cancer Center & Research Institute, in Tampa, and Puerto Rico Cancer Center received a $375,000 three-year program planning grant from NCI to form a partnership. The P20 grant is part of a program designed to promote interactions between NCI-designated cancer centers and minority-serving cancer centers. As part of the study criteria, Moffitt investigators are paired with investigators in Puerto Rico, allowing each physician or researcher to share information relevant to his or her particular specialty, said **Scott Antonia**, one of the MCC investigators involved in the study. "Minority-serving cancer centers are underrepresented, particularly in clinical trials," said **Teresita Munoz-Antonia**, investigator with the Moffitt Molecular Oncology Program. "We seek to enhance the Puerto Rico Cancer Center's treatment and research programs and build a partnership that is mutually beneficial." . . . **SUSAN SIEBER**, a former NCI official who retired last September as director of the NCI Office of Communications, died Jan. 22, following a recurrence of breast cancer. Sieber oversaw the reorganization of NCI's

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violations of the federal security laws."

SEC does not announce inquiries or comment on them. However, the agency disclosed the probe in a letter requesting a copy of the Jan. 4 issue of **The Cancer Letter**. "We are trying to determine whether there have been any violations of the federal security laws," the SEC stated in the letter dated Jan. 16. "The investigation does not mean that we have concluded that anyone has broken the law."

An informal inquiry, unlike a formal inquiry, does not have the power to subpoena witnesses and documents. Attorneys familiar with SEC practice say an informal investigation can become formal as soon as investigators encounter a need to subpoena, and in some cases, the agency proceeds directly from an informal inquiry to filing charges.

The news of a Congressional investigation sent ImClone stock into another tailspin. On Jan. 23, the price of ImClone shares hovered around $20 per share, about a third below its value a week earlier. Last September, Bristol bought a 20-percent stake in the company at $70 per share, paying a total of $1 billion. ImClone is facing over a dozen suits from disgruntled shareholders.

ImClone Chief Operating Officer Harlan Waksal said the company will cooperate with the Congressional investigation.

"We were very surprised to hear of that investigation," Waksal said Jan. 23, at a Morgan Stanley teleconference for investors. "But on reflection, it may be a good opportunity for the company to go ahead and clear the air on many of the issues that have been raised, primarily by the media, and picked up by various groups, resulting in various efforts like this Congressional investigation."

Last month, FDA sent ImClone a "refusal to file" letter, which stated that the company's clinical data on C225, trade name Erbitux, could not be interpreted, and therefore were not suitable for presentation to the agency's Oncologic Drugs Advisory Committee. The company sought accelerated approval for a combination of C225 and CPT-11 as a treatment for colorectal cancer in patients refractory to other regimens containing CPT-11.

A copy of the refusal-to-file letter, obtained by **The Cancer Letter**, stated that the agency could not verify that patients enrolled in the company's pivotal trial were indeed refractory to CPT-11, and that the overall structure of the company's phase II trial made it impossible to determine how each of the two drugs affected the safety and efficacy of the regimen (**The Cancer Letter**, Jan. 4, Jan. 11).

The letters launching the Congressional probe were signed by Energy and Commerce chairman Billy Tauzin (R-LA), and Oversight and Investigations chairman James Greenwood (R-PA), and addressed to FDA acting commissioner Bernard Schwetz, ImClone Systems President and CEO Samuel Waksal, and BMS chairman and CEO Peter Dolan.

The most detailed of the three letters was addressed to FDA's Schwertz.

"Available information seems to conflict with ImClone's descriptions of the contents of FDA's refusal-to-file letter and its clinical research," the Tauzin-Greenwood letter to Schwertz states. "The RTF letter is not a public document; investors only learned about the details from the excerpts of the RTF letter reported in **The Cancer Letter**. Without **The Cancer Letter** article, investors would have had to rely on ImClone's questionable descriptions of the RTF letter."

The Tauzin-Greenwood letter noted that by law, FDA is precluded from disclosing RTF letters and other information potentially involving trade secrets to SEC or other agencies that are not part of HHS. "For the sake of protecting patients and investors from deception, we are interested in learning whether FDA

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laws need to be clarified to permit the FDA on its own accord, and in appropriate circumstances, to share non-public information with other federal agencies," the letter states.

The Tauzin-Greenwood letter asked FDA to provide information that would allow the committee investigators to determine whether ImClone insiders knew that their clinical development program would not meet the regulatory standards for accelerated approval.

"We are interested in learning about the true nature of the pivotal clinical trial for Erbitux, and whether ImClone knew or should have known about the insufficiencies detailed in FDA's RTF letter," Tauzin and Greenwood wrote. "It is important that the hopes of cancer patients are not falsely raised and that the integrity of biomedical research is maintained."

At the Morgan Stanley conference, Harlan Waksal declined to comment on all matters involving SEC. "We are not privy to FDA policy on sharing materials with the SEC, and as a matter of policy, we just don't comment on discussions with government agencies, but we are always happy to provide the SEC with any information that it may deem useful to assure that we are in full compliance with SEC regulations," he said.

"The Furthest Along Of New Treatments"

The text of the Tauzin-Greenwood letter to FDA follows:

The Subcommittee on Oversight and Investigations is investigating questions about the conduct of ImClone Systems Inc. in the development of its colorectal cancer drug, Erbitux (also known as C225 or Cetuximab).

ImClone Systems and Erbitux are internationally known, having been featured on the CBS program 60 Minutes and the international cover story for the July 30, 2001, issue of Business Week. One reason Erbitux received such attention is that, according to Business Week, this drug was "the furthest along of a handful of new cancer treatments that precisely home in on a growth signal found in up to 50 percent of all cancer types."

In clinical trials, "the drug demonstrated remarkable success in causing colon cancer to regress in patients who had failed to respond to all other treatments." Such promise apparently prompted thousands of cancer patients to try to obtain Erbitux either through clinical trial enrollment or "compassionate use" access. For example, USA Today reported that ImClone had received 400 calls a day from patients desperate to get Erbitux outside clinical trials.

In September 2001, Bristol-Myers Squibb bought 20 percent of ImClone for $1 billion, and agreed to pay as much as $1 billion more to obtain the marketing rights to Erbitux. On Oct. 30, 2001, ImClone submitted its Biologics License Application for Erbitux. On Dec. 17, 2001, ImClone was one of seven biotechnology companies included for the first time in the Nasdaq 100 index. Excitement and confidence in ImClone was reflected in such media reports as a Reuters article in the Dec. 26, 2001, Los Angeles Times, which proclaimed, "Erbitux, a colon cancer treatment from ImClone Systems Inc., is set to make one of the biggest splashes of 2002."

Therefore, many observers were stunned to learn that on Dec. 28, 2001, the FDA had issued a "refuse-to-file" (RTF) letter in response to the ImClone submission. The RTF letter, sent in rare cases when a submission is deemed insufficient, is a non-public document containing trade secret or confidential commercial information.

According to Adam Feuerstein's column in TheStreet.com, in "its Dec. 31, 2001 conference call, ImClone executives said that FDA regulators sent the RTF letter because the Erbitux application was missing certain 'train of documentation' information needed by regulators to accept the filing. ImClone said it would be able to answer the FDA questions by the end of the first quarter, leading, hopefully to an approval of Erbitux in the fall." On the first trading day after the issuance of the RTF letter, ImClone's shares fell $11.15, or 20 percent, to $44.10 per share.

On Jan. 4, 2002, **The Cancer Letter** published excerpts of the RTF letter, indicating that the FDA had greater concerns about ImClone's data than company executives stated in the Dec. 31 conference call with analysts and investors.

As Adam Feuerstein noted, "if **The Cancer Letter** does have a correct copy of the RTF letter, it suggests that ImClone executives have not given investors and Wall Street analysts a full picture of the Erbitux problems."

The Cancer Letter article reported that the RTF letter detailed a long list of FDA concerns that went far beyond record-keeping. The FDA was quoted as saying that ImClone's clinical trial was "not adequate and well controlled," and that additional studies would be needed. Moreover, the letter suggested that the FDA had warned ImClone starting in August 2000 that its

data would have to demonstrate that Camposar, another cancer drug, was needed along with Erbitux.

But the data submitted by ImClone was not sufficient to distinguish the effects of Campostar and Erbitux. Furthermore, the FDA cited protocol violations in the clinical trial, specifically the fact that ImClone only reported the deaths of three patients who died within a month of their last Erbitux treatment.

The FDA found 21 patients who died within a month of their last Erbitux treatment. According to the Jan. 8, 2002, New York Times, David Hines, president of the Avalon Research Group, said, "The FDA's communications with the company appear directly at odds with the statements made by the company in 2001." After **The Cancer Letter** report appeared, the price of ImClone shares fell further to open on January 7, 2002 at $34.96 per share.

On Jan. 9, 2002, after ImClone had lost nearly $1.5 billion in market value since Dec. 28 and after the filing of at least 11 federal class action suits, Sam Waksal, the ImClone president and CEO, attempted to explain the company's situation at the J.P. Morgan H&Q Healthcare conference. "What happened was that we put together a faulty package, and we screwed up," Waksal reportedly said. The principal problem, he said, was the company's failure to provide documentation demonstrating that the patients enrolled in ImClone's pivotal trial had met the eligibility criteria.

On Jan.11, 2002, the **The Cancer Letter** published an article on the conference and raised more questions about Waksal's explanations of what went wrong. For example, Waksal said that the problems were caused by the Independent Response Assessment Committee (IRAC), a group of two radiologists and two oncologists, who reviewed the data from the trial's sites.

However, **The Cancer Letter** article cites Howard Ozer, director of Oklahoma University Cancer Center and Eason chair of oncology and hematology, who said blaming the review committee is disingenuous. "It is not the IRAC's fault," said Ozer, who reviewed the RTF letter for **The Cancer Letter**. "IRAC would have done whatever they were asked to do." The committee was working for the company, which means that the company bears the ultimate responsibility, Ozer said. "They would know when IRAC is screwing up, and they would immediately report back," Ozer said. "Companies do it in self-defense, so this kind of thing doesn't happen."

Adding to the controversy are sales of stock by ImClone executives in the weeks just before FDA issued the RTF letter. According to the Jan. 9, 2002, Wall Street Journal, ImClone's Chief Operating Officer, Harlan Waksal, disposed of 700,000 ImClone shares on Dec. 6, valued at roughly $71 a share or about $50 million in total.

On Oct. 29, 2001, ImClone executives and directors sold a combined 2.1 million company shares to Bristol-Myers for $150 million. Samuel Waksal sold 814,674 shares and Harlan Waksal sold 776,450 shares, or just more than 20 percent of each of their holdings, in the first sale by either executive since the mid-1990's. The sales were part of a tender offer by Bristol-Myers at the end of October in connection with the strategic agreement with ImClone. (In contrast to the $2 billion agreement with Bristol-Myers for the US market, we note that it appears ImClone made only a $60 million agreement with Merck KGaA for the right to market Erbitux outside North America and Japan, according to ImClone's 10-Q SEC filing).

As part of the tender offer, the Waksals and other insiders—along with all other shareholders—were allowed to tender shares. However, according to the Wall Street Journal, ImClone lent money to insiders so they could acquire shares through the exercise of options at a time when discussions with Bristol-Myers "were well under way (having started in May) but weren't publicly disclosed."

Along with the Waksals, ImClone extended loans to the company's chairman and another director, totaling $35.2 million during July and August. As one observer noted in the Wall Street Journal article, that select insiders were able to borrow money from the company in order to acquire shares "puts shareholders at a disadvantage."

Given these recent reports, we have several serious concerns. Available information seems to conflict with ImClone's descriptions of the contents of FDA's RTF letter and its clinical research. The RTF letter is not a public document; investors only learned about the details from the excerpts of the RTF letter reported in **The Cancer Letter**. Without **The Cancer Letter** article, investors would have had to rely on ImClone's questionable descriptions of the RTF letter.

The FDA's statute and regulations appear to inhibit the agency on its own from disclosing some, if not all, of the RTF letter or other similar, relevant information to the Securities and Exchange Commission (SEC) when there are concerns about the accuracy and completeness of company's descriptions of FDA actions. We note that Section

301(j) of the Federal Food, Drug, and Cosmetic Act prohibits the "revealing, other than to the Secretary or officers or employees of the Department . . . any information . . . concerning any method or process which as a trade secret is entitled to protection."

Therefore, according to FDA's Regulatory Procedures Manual, FDA may not share trade secret information with federal government agencies outside the Department of Health and Human Services unless the submitter of the trade secret consents in writing. Under 21 C.F.R. section 20.85 any FDA records exempt from public disclosure may be disclosed to other Federal government departments and agencies, except that trade secrets and confidential commercial or financial information prohibited from disclosure by 21 USC 331(j) . . . may be released only as provided by these sections. For the sake of protecting patients and investors from deception, we are interested in learning whether FDA laws need to be clarified to permit the FDA on its own accord, and in appropriate circumstances, to share non-public information with other federal agencies.

We are also interested in learning about the true nature of the pivotal clinical trial for Erbitux, and whether ImClone knew or should have known about the insufficiencies detailed in FDA's RTF letter. It is important that the hopes of cancer patients are not falsely raised and that the integrity of biomedical research is maintained. The available information demands that this Committee, which is entrusted with the oversight of public health and consumer protection laws, get additional information about ImClone and the Erbitux matter.

In light of these concerns, pursuant to Rules X and XI of the U.S. House of Representatives, please provide the following by January 31, 2002:

1. All records relating to the December 28, 2001 refusal-to-file letter for ImClone Systems' biological license application for Erbitux.

2. All records relating to meetings between FDA and ImClone Systems concerning Erbitux.

3. All records relating to study CP02-9923, especially the study protocol.

4. All records relating to communications about the biological license application for Erbitux since October 29, 2001.

5. The most current legal analysis of relevant federal statutes and regulations concerning FDA disclosure of non-public information to the Securities and Exchange Commission (SEC). If no such analysis exists, please provide an explanation to the Committee of the circumstances, and for what categories of non-public information, that FDA on its own initiative may provide to the SEC. Please advise the Committee on whether FDA has had contact with the SEC on the ImClone/Erbitux matter and, if there was contact, appropriate details about the nature of the contact.

In a separate letter, the committee asked ImClone President and CEO Samuel Waksal to provide the following documents:

—All records relating to communications about the FDA's Dec. 28, 2001, refusal-to-file letter.

—All records relating to meetings between FDA and ImClone Systems concerning Erbitux.

—All records relating to study CP02-9923, especially the study protocol. Please identify the ImClone official responsible for coordinating with the Independent Response Assessment Committee. Please provide a list of all outside consultants or experts used by ImClone for study CP02-9923.

The letter to BMS chairman and CEO Dolan requested the following:

—All records relating to communications about the FDA's Dec. 28, 2001, refusal-to-file letter regarding ImClone's Erbitux.

—A list of the individuals involved in Bristol-Myers Squibb's (BMS) due diligence review of ImClone Systems. Please describe how BMS organized its due diligence efforts regarding ImClone Systems.

—Internal audits, internal investigations, and/or reports relating to ImClone Systems.

—Did BMS draw on the expertise of its Oncology Advisory Board to assess the Erbitux data before the ImClone deal was completed? If not, why not? What information did BMS rely on in assessing the Erbitux data?

—All records relating to the Oct. 26, 2001, briefing before the BMS Oncology Advisory Board concerning Erbitux.

Andrew von Eschenbach Sworn In As NCI Director

Andrew von Eschenbach was sworn in as the 12th director of NCI on Jan. 22 in an informal ceremony in his office.

A representative from HHS Secretary Tommy Thompson's office and NCI officials and staff were in attendance.

The new director planned to meet with NCI staff over the next few days. A formal swearing-in

ceremony is scheduled for Feb. 4, sources said.

Von Eschenbach, a urologic surgeon from M.D. Anderson Cancer Center in Houston, was appointed by President Bush late last year to replace Clinton appointee Richard Klausner, who stepped down last September (**The Cancer Letter**, Dec. 7, 2001, Vol. 27 No. 45).

"I am extremely honored and excited to accept this important role," von Eschenbach said in remarks posted on the NCI Web site. "I intend to access all the expertise from this great institute of knowledge, and experience and from experts throughout the community, in order for us to work collaboratively and collectively towards a comprehensive solution to the problem of cancer."

Following are excerpts of an interview of von Eschenbach by Michael Miller, of the NCI media branch:

Q: Are there any major, overall goals you'd like to achieve during your tenure at NCI?

A: I have told former NCI Director Richard Klausner that I am coming to the NCI to complement the previous Directors, and I mean that as both complement and compliment. I compliment them for the tremendous accomplishments and progress the NCI has achieved under their leadership. Since the passage of the National Cancer Act 30 years ago, we have made great progress in our scientific understanding of the biology of cancer. We have much more to learn about this complex disease, but the National Cancer Institute has been responsible for many of these accomplishments. At the same time, I see a responsibility to complement what's gone before by building on that foundation. Our emerging understanding of cancer at the genetic, molecular, and cellular levels opens up enormous opportunity to alter disease processes at each level. The paradigm that I grew up with as an oncologist was to 'find cancer and kill it'. Now we can look forward to not only eradicating cancer, but to 'target and control it' by modulating and altering the behavior of cancer. Our goal should be to accelerate the evolution of this exciting new paradigm, leading to biology-based interventions to detect, treat, and prevent cancers.

Q: You've been through treatment for cancer yourself twice. Do you feel this experience has influenced you in your roles as cancer researcher and administrator?

A: Clearly having cancer has affected me, however I don't think you have to be a cancer patient to be a compassionate oncologist or a researcher passionate about a cure. Developing cancer did not make me more compassionate or more passionate, but rather gave me more of a sense of urgency. I initially made the decision to be an oncologist because, intellectually, the mysteries of cancer fascinated me the most. But then during my urology residency, my dad was diagnosed with prostate cancer and later, as I was practicing oncology full-time in the clinic, I witnessed first-hand cancer's tremendous everyday toll in human suffering. Being a cancer physician requires caring and dedication. Being a cancer patient brings with it a deep sense of urgency about eradicating this disease. It is important to not just solve the problem, but to solve it as quickly as possible, because every day that we don't is another day that people suffer and die. So I appreciate the balance between being careful, meticulous, and precise in our research, but at the same time I will drive this process with a sense of urgency. I will always maintain that the cancer patient is at the center of what we're doing. Ultimately, what we accomplish will be measured in terms of people living or dying or suffering or not.

Q: You've served in important leadership capacities for both the American Cancer Society and the National Dialogue on Cancer. How do you see these and other such organizations interacting with the NCI, and what can NCI do to foster good relations with these and other cancer support organizations?

A: The role that the NCI has played in what we may call the National Cancer Agenda has been crucial and can even be thought of as the keystone. The NCI plays a critically important part in fostering research and promoting the delivery of state-of-the-art care. Increasingly, many other organizations and agencies are playing essential roles, especially in delivery of care. The Food and Drug Administration, CDC, CMS (formerly HCFA), state agencies, and health care delivery systems and providers, are essential to insure an ultimate solution to the problem of cancer. The NCI can't provide for everything that is required for a successful National Cancer Agenda, but it must play a key leadership role in making sure the agenda is fulfilled. Cooperation, collaboration, and integration are very important and the NCI will continue to forge creative partnerships with many other organizations at the federal, state, and local levels as well as pharmaceutical and biotechnology companies, cancer survivor groups, and non-governmental groups like the American Cancer Society, the American Association for Cancer Research, the American Society of Clinical Oncology, and others.

Q: Unlike a number of former NCI Directors, you've had no formal Federal government employment. How do you think your experience as a government official will differ from your experience in the academic sector?

A: Although I've not been at NCI, I've spent many years at M.D. Anderson Cancer Center, a state institution, which is a part of the University of Texas. I do have an understanding of a governmental system and its rules, regulations, and processes. I am blessed by the fact that I'm surrounded by people at the NCI who understand the system exceedingly well. Deputy Director Alan Rabson has been at NCI for 46 years and is invaluable to have at my side. I also have an Executive Committee made up of individuals with great experience and I'm looking forward to working and interacting with them.

New Web Site Design

In a press release dated Jan. 22, NCI also announced the launch of its "dramatically improved, easy-to-navigate Web site, Cancer.gov (http://cancer.gov), a one-stop resource for cancer information."

The new site has reorganized CancerNet and cancerTrials, into Cancer.gov's Cancer Information and Clinical Trials portals.

New Logo, Tagline Dropped

According to NCI sources, the Institute was to have unveiled a new logo at the same time as the redesigned Web site.

The logo was "introduced" to NCI Office of Communications staff at a Nov. 6 meeting, according to a staff bulletin.

The logo and Web site were part of NCI's "branding" project begun more than a year ago and given significant resources for focus-group research and design development.

At one point, the communications office held a contest for staff to come up with a new "tagline," or motto.

NCI's new tagline, to be unveiled with the logo, was to have been: "The Power of Research, The Promise of Hope."

This tagline received "positive ratings from both the scientific community and the general public," according to an NCI internal bulletin.

NCI's communications office was reorganized over the past year ostensibly to improve coordination between the various communications functions of the Institute. However, the logo was developed by one group, while the new Web site design was developed by another, sources said.

Late last year, it was all to have come together for a meeting of the NCI Executive Committee. The new logo was pasted into the new Web site pages for a demonstration for the Institute's top officials.

The logo and the site pages didn't match. The Web site pages left about a 1-inch by one-half inch space for the logo. The logo looked clunky, sources said.

The Executive Committee nixed it.

Funding Opportunities:

NCI RFA Available

RFA-CA-03-001: Cooperative Grants for Nutritional Modulation of Genetic Pathways Leading to Cancer

Letter of Intent Receipt Date: June 14, 2002

Application Receipt Date: July 12, 2002

NCI invites applications to develop cooperative specialized centers for both basic and clinical research in areas related to dietary nutrients as modifiers of genetic pathways leading to cancer. The RFA invites investigators to form interdisciplinary research teams to resolve complex gene-nutrient interrelationships that relate to cancer prevention. All research approaches are encouraged, as long as they address the following essential features: a cancer focus, institutional commitment, organizational capabilities, facilities, and interdisciplinary coordination and collaboration. Receipt of a Planning Grant award P20 is not a prerequisite to apply for the RFA. A team must include investigators from one or more institutions with expertise in nutrition and molecular biology/ genetics and may contain others as required to address the role(s) of nutrient(s) on genetic pathways leading to cancer.

Examples of areas of interest include, but are not limited to carcinogen bioactivation, cell-cycle control, signal transduction; intercellular communication, apoptosis; immune effectors, and angiogenesis. An informational session for investigators planning to submit applications in response will be held Tues., Feb. 19, 2002, from 1:00 PM to 3:00 PM at the Bethesda Marriott, 5151 Pooks Hill Road, Bethesda, MD 20814. The RFA will use NIH U54 award mechanism. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-03-001.html.

Inquiries: John Milner, chief, Nutritional Science Research Group, DCP, NCI, Executive Plaza North, 6130 Executive Blvd, EPN Suite 3164, Rockville, MD 20852, e-mail milnerj@mail.nih.gov; phone 301-496-0108; fax 301-480-3925.

Program Announcement

PA-02-048: Dissertation Research Grants for Underrepresented Minorities in the Ethical, Legal and Social Implications of Genetic Research

Applications may be made for support of research in any area relevant to the ethical, legal and social implications of genetic and genomic research. Proposed projects can range from large clinical studies of the impact of genetic information and technologies in health care settings to smaller analytical studies of how this information affects individuals or how communities view themselves or are viewed by others.

General areas of programmatic interest are set out on the NHGRI ELSI Research website at http://www.nhgri.nih.gov:80/About_NHGRI/Der/Elsi/.

Five research goals have been developed for the NHGRI ELSI program through the year 2003: 1. Examine the issues surrounding the completion of the human DNA sequence and the study of human genetic variation. 2. Examine issues raised by the integration of genetic technologies and information into health care and public health activities. 3. Examine issues raised by the integration of knowledge about genomics and gene-environment interactions into non-clinical settings. 4. Explore ways in which new genetic knowledge may interact with a variety of philosophical, theological, and ethical perspectives. 5. Explore how the social environment, including socioeconomic factors, age, gender and concepts of race and ethnicity influence the use, understanding, and interpretation of genetic information, the utilization of genetic services, and the development of policy. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-02-048.html.

Inquiries: Jean McEwen, ELSI Research Program, National Human Genome Research Institute, Bldg. 31, Rm B2B07, 31 Center Dr, MSC 2033, NIH, Bethesda, MD 20892-2033, phone 301 402-4997; fax 301-402-1950; e-mail jm522n@nih.gov

Other Funding Notices

NOT-OD-02-028: National Research Service Award Stipend Increase and Other Changes Effective for Fiscal Year 2002

NRSA stipend levels for predoctoral and postdoctoral trainees and fellows have increased for fiscal 2002. Also, training-related expenses for trainees and the institutional allowance for individual fellows are being increased. The notice is available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-028.html.

Inquiries: Walter Schaffer, research training officer, NIH, 6701 Rockledge Dr., Rm 6184, Bethesda, Maryland 20892-7911, phone 301-435-2687; fax 301-480-0146; e-mail ws11q@nih.gov

In Brief:

Susan Sieber, Former NCI Communications Chief, Dead

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communications branches. She served in a variety of positions in her 30-year career at NCI, including as deputy director of the Division of Epidemiology and Genetics and deputy director of the Division of Cancer Etiology. . . . **CANCERTRIALSHELP.ORG**, a Web site operated by the Coalition of National Cancer Cooperative Groups, a nonprofit based in Philadelphia, opened an Employer Resources section of the site. The section provides education and practical information, including summaries of the current state of insurance coverage for cancer clinical trials. "Employers are an important source of information, particularly about insurance coverage, for workers who are diagnosed with cancer," said **Robert Comis**, president of the Coalition. "By equipping employers with the facts about cancer clinical trials, we can help them help their employees and ultimately raise awareness and, hopefully, participation in clinical trials." CancerTrialsHelp.org is dedicated to advancing the awareness of cancer clinical trials. . . . **NATIONAL FOUNDATION** for Cancer Research said scientists at the NFCR Center for Computational Drug Design at Oxford University have teamed with technology companies Microsoft, Intel, and United Devices to help discover new drugs to combat the anthrax virus. The initiative uses the same technology platform as the "Cure Cancer with your Computer" project that turns personal computers around the world into a virtual supercomputer. Personal computer users may download software that enables researchers to tap into their unused computer power. The download can be found at http://www.Researchforacure.com or at http://www.Intel.com/Cure. A software program called "THINK" runs anthrax protein and molecule structures and then coordinates the application of a computer's screen saver time to run binding tests on an individual's computer. The applications then send the compiled research data to computer servers in Europe and then assign the computer another molecule to examine. The project is expected to last three to six months. "We continue to identify the short and long term benefits of distributed computing in our efforts to discover more efficient and speedy ways to identify new drug candidates," said **Graham Richards**, director of the NFCR Center for Computational Drug Design at Oxford University.

THE CANCER LETTER

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Business & Regulatory Report

Clinical Trials:

Control-Arm CML Patients In Phase III Gleevec Study Allowed To Switch

In an interim analysis of the ongoing phase III study comparing Gleevec (imatinib mesylate) to standard therapy (interferon injections plus Ara-C [cytarabine] chemotherapy) for initial treatment in newly diagnosed CML patients, the Gleevec arm was found to demonstrate a substantially higher response.

An Independent Data Monitoring Board comprised of independent hematologists and a clinical statistician recommended a change in the protocol to enable the patients on standard therapy who have not achieved

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Deals & Collaborations:

Amgen Agrees To Buy Immunex For $16 Billion In Stock And Cash

Amgen (Nasdaq: AMGN) of Thousand Oaks, CA, and **Immunex Corp.** (Nasdaq: IMNX) of Seattle, said they have signed an agreement for Amgen to acquire Immunex for $16 billion in stock and net cash.

Under the agreement, each share of Immunex common stock will be exchanged for a fixed-ratio of 0.44 shares of Amgen common stock, and cash of $4.50, or a total of 85 percent in stock and 15 percent in cash, the companies said.

Amgen will have pro forma 2002 revenues of $5.5 billion and 2002 net income in excess of $1.5 billion.

"By accelerating our strategic and financial plan, this transaction creates a tremendous opportunity for Immunex shareholders to participate in the clear potential of this biotech powerhouse," said Ed Fritzky, chairman and CEO of Immunex, who will join the Amgen board of directors. "The strength of this combination lies in expanding future patient benefits by harnessing the significant resources, talents and assets of these two leading organizations."

Under the agreement, each share of Immunex common stock will be exchanged for a fixed-ratio of 0.44 shares of Amgen common stock and cash of $4.50, or a total of 85 percentage in stock and 15 percentage in cash, the company said. Amgen will acquire Immunex in a tax-free reorganization, and the Immunex shareholders will not be taxed to the extent that they exchange their Immunex stock for Amgen stock. Amgen shareholders will own 81 percent of the new company and Immunex shareholders will own 19 percent. As part of the agreement, Amgen will

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Higher Response To Gleevec Found In Phase III Trial

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a major cytogenetic response to switch to Gleevec.

Gleevec is marketed by Novartis Oncology of East Hanover, NJ, a unit of Novartis AG (NYSE: NVS).

The change in the protocol was communicated to investigators and patients beginning Jan. 3 and allows patients on the control arm who have not achieved a major cytogenetic response after one year of treatment with interferon-alpha and cytarabine to switch to Gleevec, the company said.

According to the company, consent forms will be changed to inform patients of the new data, and to urge them to speak with their physicians.

Called the IRIS study (International Randomized study of Interferon vs. STI571), the phase III trial is evaluating Gleevec vs. the combination of standard interferon and cytarabine as first line therapy in patients with CML. Between June 2000 and January 2001, the study enrolled 1,106 patients in 177 centers across 16 countries. The study was designed to help determine the long-term outcome, including survival, of patients with newly diagnosed CML , the company said.

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Ekips Technologies Inc. of Norman, OK, said the University of Oklahoma Health Sciences Center institutional review board has approved a clinical trial of a breath test for early diagnosis of lung cancer.

Principal investigators will be Jean Keddissi and Alain Eid of the OUHSC Pulmonary and Critical Care Group and William Potter, associate professor of chemistry at the University of Tulsa, the company said. The trial will be conducted at the OU Medical Center in Oklahoma City.

"During the past two decades, researchers have found hundreds of different elements of human breath, which can be used to diagnose chronic illnesses," said Keddissi. "If we can identify specific combinations of biomarkers that are linked to lung cancer, the technology can rapidly display the result through the use of its highly sensitive laser technology. Our goal is for the laser technology to eventually replace lung volume measurement and other indirect testing as a screening and monitoring tool for a number of pulmonary diseases."

Patrick McCann, founder and president of Ekips Technologies and professor of electrical engineering at the University of Oklahoma, developed the Ekips Breathmeter, a laser-based breath-testing machine for asthma, the company said.

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Medarex Inc. (Nasdaq: MEDX) of Princeton, NJ, said its multi-pronged tumor vaccine program for a variety of tumors, including advanced or incurable malignant melanoma are in phase I/II trials.

The program uses a series of different melanoma vaccines used together with MDX-010, a fully human antibody that binds to CTLA-4, a molecule associated with the suppression of normal immune responses to cancer, the company said. The company said it is testing MDX-010 with two different melanoma vaccines, with additional vaccines expected to enter clinical trials during 2002.

CTLA-4 is a T-cell molecule that ordinarily provides a negative signal to the immune system, the company said.

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Millennium Pharmaceuticals Inc. (Nasdaq: MLNM) of Cambridge, MA, said it has begun multiple phase I trials of MLN341 (formerly LDP-341, PS-341), in combination with Taxotere (docetaxel), for injection concentrate for breast and lung cancers.

The studies will assess the safety of MLN341 in combination with the commonly used cancer agent in advanced solid tumors, the company said.

MLN341, is a small molecule proteasome inhibitor under development for treat human

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malignancies, the company said.

"Millennium continues its aggressive MLN341 clinical development program with a variety of phase I and phase II trials underway in solid tumors and hematologic malignancies as both a single agent and in combination," said Michael Kauffman, vice president, medicine and MLN341 project leader at Millennium. "We anticipate the start of a phase III trial in multiple myeloma later this year."

The trials are taking place at the Cleveland Clinic and Vanderbilt University Medical Center in prostate cancer and the California Lung Consortium in lung cancer, the company said. An additional trial in breast cancer is scheduled to begin in the first quarter at several European sites. The combination trials are open label, dose escalation studies of MLN341 plus Taxotere in patients with advanced solid tumors. The goal of the studies is to assess the safety and determine the maximum tolerated dose of the MLN341/Taxotere combination.

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Myriad Genetics Inc. (Nasdaq: MYGN) of Salt Lake City said it has submitted to FDA a multi-center, double-blind, placebo-controlled clinical trial of its prostate cancer drug, Flurizan (MPC-7869) at 65 sites in the U.S.

Four hundred early-stage prostate cancer patients will be enrolled to evaluate systemic disease progression of prostate cancer, the company said. Patients will be assigned to one of three regimes (either one of two different doses of Flurizan or placebo). The primary clinical endpoints for the trial include time to metastases and effect on prostate specific antigen levels. To date, two phase I trials and one phase IIa trial have been completed in healthy volunteers and late-stage cancer patients, which demonstrated encouraging results in safety, bioavailability and pharmacokinetics, the company said.

Flurizan affects a drug target in a pathway involved in the regulation of NFkB, a transcriptional activator implicated in cancer and inflammatory diseases, the company said.

Myriad said it is further elucidating the complete biological pathway around the drug target, upon which Flurizan acts, using its proprietary pathway technologies, including ProNet and ProSpec. Four issued U.S. and foreign patents cover Flurizan and an additional nine patents are pending worldwide.

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NewBiotics Inc. of San Diego said it has begun a phase I/II clinical trial of NB1011 for colon cancer.

Developed under a joint venture with **Elan Corp**., NB1011 is the first product derived from the NewBiotics ECTA (enzyme catalyzed therapeutic activation) technology, the company said.

NB1011 targets TS as a substrate rather than an inhibitor, the company said. Like the Trojan Horse of ancient Greece, NB1011 appears harmless as it enters a diseased cell but is converted into a toxin by the target enzyme. Preferential tumor toxicity should be achieved since TS is elevated in cancer cells compared to normal cells. Preclinical studies in animals indicate the drug candidate has activity against both drug-resistant and non-resistant tumors derived from human colon and breast cancer with no detectable toxicity to the animal.

Phase I will examine pharmacokinetics and establish a maximum tolerated dose of NB1011 in drug-resistant metastatic or relapsed colon cancer, the company said. During phase II, patients will be treated at the MTD dosage to continue assessing safety and clinical anti-tumor activity of the compound.

The trial will be conducted at UCLA and USC cancer centers, respectively, the company said. Mark Pegram and Heinz-Josef Lenz will lead the study.

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SciClone Pharmaceuticals (Nasdaq: SCLN) of San Mateo, CA, said it has begun a late-stage oncology clinical development program sponsored by **Sigma-Tau S.p.A**., the SciClone exclusive partner in the European Union, for Zadaxin, an immune system enhancer for malignant melanoma.

The Sigma-Tau phase II trials are based on the success of a smaller open label study conducted in the EU by independent researchers, the company said. In that study, 10 of 20 late-stage patients showed a complete or partial response when the drug was added to the standard combination therapy, dacarbazine and alpha interferon. The median survival was 11.5 months, a clinically significant increase over the standard treatment's historical efficacy.

Under the collaborative agreement, and in addition to funding the European oncology clinical program, Sigma-Tau said it has agreed to make $3.7 million in payments to SciClone to help fund the U.S. hepatitis C trials. SciClone expects to receive the initial $2.7 million milestone payment prior to the end of 2001 for work already completed in its U.S. hepatitis C trial program and to receive a $1 million milestone payment upon completion of U.S. patient enrollment. Sigma-Tau has exclusive rights for EU clinical

development, registration, marketing and sales of Zadaxin, the company said. SciClone retains all U.S. and other international rights to the drug.

Zadaxin is a pure synthetic preparation of thymosin alpha 1, a peptide that helps stimulate, maintain and direct anticancer responses, the company said.

Oncology Management:

Amgen To Buy Immunex In Reorganization

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acquire the 41 percentage stake in Immunex held by **American Home Products Corp.** (NYSE: AHP), for the same purchase price per share, giving AHP an 8 percentage stake in the new company. AHP has agreed to vote in favor of the transaction.

The transaction is anticipated to close in the second half of 2002, subject to approval by shareholders of both companies, as well as regulatory approvals, the company said.

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Access Oncology Inc. of New York said its pharmaceutical subsidiary entered into a licensing agreement with **Gem Pharmaceuticals Inc.** of Birmingham, AL, for GPX-100 and GPX-150, two, non-cardiotoxic analogs of doxorubicin.

The agreement calls for Access to fund all future development plus pay upfront payments and development milestones of up to $33 million followed by royalties on sales of approved products, the company said. AO will have exclusive licensing rights in all markets except for Asia, which has been retained by Gem.

GPX-100 is a non-cardiotoxic analog of doxorubicin, a chemotherapy for breast cancer, the company said. Doxorubicin's clinical utility is limited because it causes cardiac damage that can progress to fatal congestive heart failure. Gem scientists identified GPX-100, which has been shown in preclinical studies to maintain the anti-cancer effects of its parent compound, doxorubicin, while virtually eliminating chronic cardiotoxicity. Based on its mechanism of action and pre-clinical data, GPX-100 may have significant utility in the treatment of breast cancer, sarcoma and certain hematological cancers.

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Atrix Laboratories Inc. (Nasdaq: ATRX) of Fort Collins, CO, said **Sanofi-Synthelabo** exercised its right to develop a dosage form of Leuprogel.

Atrix is in late stage development for three other Leuprogel products for prostate cancer, which will be marketed by Sanofi-Synthelabo in the U.S. and Canada following FDA approval.

Under the agreement, Atrix will receive reimbursement for research and development expenses related to the development of the Leuprogel dosage form and expects to submit an investigational new drug application to FDA this year, the company said. Atrix will receive payments for certain regulatory and sales milestones, a royalty based on sales of the product and will manufacture the Leuprogel products at its facility in Fort Collins, CO.

Atrix has submitted new drug applications to FDA for the approval of Leuprogel One-Month and Three-Month Depot products for prostate cancer, the company said.. Phase III studies are underway for the Leuprogel Four-Month Depot product. An NDA submission for the four-month sustained release product is expected to occur in the first half of 2002.

The products use the Atrigel technology to deliver a sustained level of leuprolide acetate over a period of one to several months, the company said. The liquid Leuprogel products are injected subcutaneously with a small gauge needle, forming a solid implant in the body that slowly releases the leuprolide as the implant is bioabsorbed. The goal of these products is to suppress testosterone in the body to inhibit the growth of hormone-sensitive prostate cancer.

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Cambridge Antibody Technology (Nasdaq: CATG; LSE: CAT) of Melbourn, England, and **Immunex Corp.** (Nasdaq: IMNX) said Immunex has exercised an exclusive license option for the commercialization of human monoclonal antibodies.

The exercise of the option, one of eight granted by CAT to Immunex under an agreement signed in December 2000, grants the company the exclusive right to develop human monoclonal antibodies specific for an undisclosed disease target, the company said. CAT has received a license fee and could receive milestone and royalty payments on future antibody-based products developed and commercialized by Immunex.

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CancerVax Corp. of Carlsbad, CA, said it would acquire **Cell-Matrix Incand** and the rights to monoclonal antibodies in pre-clinical development for cancer.

Cell-Matrix is a privately held biotechnology company with intellectual property and technology in

angiogenesis, the company said.

Cell-Matrix said it has licensed and developed proprietary technologies for inhibiting and stimulating angiogenesis, and has preclinical product candidates that are antibodies that bind to denatured collagen.

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Genencor International Inc. (Nasdaq: GCOR) of Palo Alto and **Seattle Genetics Inc.** (Nasdaq: SGEN) of Bothell, WA, said they have formed a strategic alliance to discover and develop a class of cancer therapeutics based on tumor-targeted enzymes that activate prodrugs.

The companies said they will share preclinical and clinical development costs and have the right to jointly commercialize any resulting products within the field. Genencor will make an equity investment of $3 million in Seattle Genetics and will also pay specific fees and milestone payments. Seattle Genetics will make milestone payments to Genencor, the companies said.

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Genzyme Corp. of Cambridge, MA, said two of its divisions have reached an agreement to transfer the rights to intellectual property and licenses related to cancer diagnostics.

Genzyme Genetics, a business unit of **Genzyme General** (Nasdaq: GENZ), has purchased these rights from **Genzyme Molecular Oncology** (Nasdaq: GZMO).

The assets include diagnostic rights to dozens of proprietary cancer markers, providing Genzyme Genetics with a pipeline, the company said.

In exchange for these rights, GZMO has received $32 million and could receive an additional $1 million in milestone payments, the company said. The transaction brings the GZMO cash balance to approximately $40 million.

Under the arrangement, Genzyme Genetics also assumes exclusive rights to intellectual property for cancer-related genes and methods in the diagnostics field, the company said. GZMO derived revenue from some of the assets through non-exclusive licensing agreements that allow the use of the genes in cancer tests. The company said it would assume the rights to existing licenses for diagnostic use of p53.

Genzyme Genetics will have diagnostic rights to cancer markers found in the future through the Genzyme Molecular Oncology antigen discovery program, the company said.

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Isis Pharmaceuticals Inc. (Nasdaq: ISIP) of Carlsbad, CA, said it has established a long-term research-scale antisense inhibitor supply agreement with **Integrated DNA Technologies Inc.** of Coraville, IO.

In the long-term supply agreement, IDT will manufacture research-scale antisense inhibitors and research reagents to Isis specifications, the company said. The agreement enables Isis to meet increasing demand for functional genomics services that its GeneTrove division provides to pharmaceutical and biotechnology customers. Isis will pay IDT $5 million toward the future purchase of antisense inhibitors from IDT. The transaction provides IDT with financing for operations expansion, the company said.

Isis said it has also expanded its existing licensing agreement with IDT on certain patents in functional genomics and for antisense drugs. The agreement eliminates milestone payments and reduces royalty rates for commercialized second-generation antisense drugs. Isis said it would pay IDT $4.9 million for the broadened intellectual property license.

Isis owns or licenses 900 issued patents covering RNA-based drug discovery and development, the company said.

In another development, Isis Pharmaceuticals Inc. said its GeneTrove division has initiated a target validation collaboration with **Chiron Corp.** (Nasdaq: CHIR).

In the partnership, Chiron gains access to the Isis antisense technology for gene functionalization and target validation and a license to specific patents within the Isis functional genomics suite of patents, the company said. Chiron said it would use the Ribonuclease H (RNase H) mechanism of action for its in-house antisense-based functional genomics program.

Specific financial terms of the deal were not disclosed, the company said.

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Matrix Pharmaceutical Inc. (Nasdaq: MATX) of Fremont, CA, said it has entered into a definitive agreement with **Chiron Corp.** (Nasdaq: CHIR) for the acquisition by Chiron of all outstanding shares of Matrix for $61 million or $2.21 per share.

The transaction would close in the first quarter of 2002, and is subject to customary closing conditions, including the valid tender of at least a majority of the outstanding Matrix shares (on a fully diluted basis), antitrust clearance, and no material adverse changes affecting Matrix or its tezacitabine program, the company said.

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Millennium Pharmaceuticals Inc. (Nasdaq: MLNM) of Cambridge, MA, and **Xenova Group** (Nasdaq: XNVA; London Stock Exchange: XEN) of Slough, UK, said they have signed a license agreement for the development and North American commercialization of the Xenova compounds, whose mechanism of action includes dual inhibition of topoisomerases I and II, for solid tumors.

The program includes three molecules; XR11576, XR5944, and XR11612, the companies said. XR11576 is an oral agent in phase I development with the first patients screened for study entry. The two additional compounds are in preclinical development.

Under the agreement, Millennium will acquire development and exclusive marketing rights to the topoisomerase program in North America in exchange for an upfront payment of US$11.5 million as well as future milestone payments and royalties following the achievement of specific development and sales goals, the companies said.

Xenova retains commercialization rights for all products arising from this topoisomerase collaboration outside the U.S., Canada and Mexico, including marketing in Europe and elsewhere. Xenova will retain responsibility for performing development activities associated with the program, which will be funded by Millennium beginning in 2003, to the end of phase II trials. Thereafter, Millennium will assume responsibility for subsequent development activities in North America and Xenova will retain development activity responsibility elsewhere.

Also, Millennium has the right to market in North America any improvements or additional products based on the same topoisomerase inhibitor technology, in which case Xenova will receive further milestones and royalties on the sales of such products, the companies said. Additional terms of the agreement were not disclosed, the companies said.

In preclinical studies XR11576 has shown an improved biological profile when compared with first generation dual topoisomerase I and II inhibitors, including oral bioavailability and a marked enhancement of potency, the company said. In preclinical studies XR5944 has demonstrated activity against human and murine tumor cell lines and has been shown to induce tumor regression in the majority of cases in a model considered to be relatively unresponsive to chemotherapy. In a further preclinical model, low doses of XR5944 induced complete tumor regression in the majority of cases and was more effective in this respect than certain currently marketed topoisomerase inhibitors. In preclinical studies, XR11612 was shown to have significant antitumor efficacy against certain cancer disease models, the companies said.

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Oxford GlycoSciences Plc (LSE: OGS; Nasdaq: OGSI) of Oxford, England, **Medarex** (Nasdaq: MEDX) of Princeton, NJ, and **Genmab A/S** (CSE: GEN and Neuer Markt: GE9D) of Copenhagen, Denmark, said they have agreed to create medical products for breast cancer.

The development effort is designed to lead to breast cancer treatments, including new antibody and vaccine therapies, and biomarkers with a multi-pronged therapeutic approach, the company said. The therapies being developed are expected to include: antibody-based products designed to destroy tumors; the anti-heparanase I antibody to prevent tumor growth; and a vaccine approach to prevent recurrences.

The first product is a fully human antibody that binds to and neutralizes the heparanase I enzyme involved in breast cancer, the company said.

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Rigel Pharmaceuticals Inc. (Nasdaq: RIGL) of South San Francisco said that its oncology drug discovery collaboration with **Johnson & Johnson Pharmaceutical Research & Development, L.L.C**. has been extended for another two years.

Under the extension agreement, Rigel will continue to validate targets discovered during the collaboration, the company said. Johnson & Johnson Pharmaceutical Research & Development will conduct high-throughput screening and medicinal chemistry to identify small molecule drugs that modulate validated targets selected for drug discovery.

Product Approvals & Applications:

FDA Approves Abbott's HER-2 DNA Probe Kit

Abbott Laboratories (NYSE: ABT) of Abbott Park, IL, said its Vysis PathVysion HER-2 DNA Probe Kit to detect the HER-2/neu gene received approval from FDA for metastatic breast cancer.

Herceptin, marketed by Genentech Inc., is a targeted monoclonal antibody treatment for women with HER-2 positive metastatic breast cancer, the company said.

The PathVysion HER-2 test is one of the first examples of genomic disease management for which a direct genetic test enables assessments of the appropriate therapy based on genetic profiles, the company said. Based on the patented FISH technology, PathVysion enables one to directly detect both the HER-2 gene and the chromosome 17 on which the gene resides. Patients with more than two copies of chromosome 17 do not represent true amplification of the HER-2 gene. Thus, the ability to simultaneously detect chromosome 17 provides a built-in control to determine true amplification of the HER-2 gene.

* * *

AstraZeneca (NYSE: AZN) of Wilmington, DL, said it has filed a supplemental new drug application with FDA for Casodex (bicalutamide), an oral, once-daily hormonal medication for early stage non-metastatic prostate cancer.

The sNDA submission is based on data from the Early Prostate Cancer Trial Program, an international program of three prospective, randomized, double blind, placebo-controlled clinical trials and includes over 8,000 patients from 23 countries, the company said. The program investigates the effect of Casodex 150 mg as an immediate or adjuvant treatment for early prostate cancer and was designed on the same premise as the adjuvant trials of tamoxifen in breast cancer.

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CancerVax Corp. of Carlsbad, CA, said it submitted an investigational new drug application to FDA for a phase II/III trial of Canvaxin vaccine for metastatic colon cancer.

The vaccine is an allogeneic, whole cell vaccine that expresses 20 known tumor-associated antigens, fourteen of which are specifically cross-reactive with colon cancer, enhancing the overall immune response to the cancer, the company said.

Results from a phase II study for stage IV colorectal carcinoma, indicated the vaccine induced specific immune responses that correlated with survival in patients with advanced colorectal cancer, the company said.

The primary endpoint will be overall survival and assessment safety and efficacy of the vaccine versus standard of care following surgical resection of the primary tumor and resection or ablation of any known metastases, the company said. Standard of care may include observation, radiation therapy, or chemotherapy as determined by the clinical trial investigator. CancerVax anticipates enrolling approximately 670 patients at 50 clinical sites in the U.S. and abroad.

The vaccine has been administered to over 2,000 patients in phase II trials that have been funded by NCI, the company said.

* * *

Human Genome Sciences Inc. (Nasdaq: HGSI) of Rockville, MD, said FDA has approved its investigational new drug application for Albuleukin, a recombinant human protein, for cancer.

HGS said it will open a multi-center, open-label, dose-escalation study to evaluate the safety and pharmacology for solid tumors.

Albuleukin is a modified form of interleukin-2, the company said. Preclinically, Albuleukin exhibits expanded tissue distribution, is longer-acting and is better tolerated, as compared with interleukin-2 itself and could be used for a broader range of cancers than the original interleukin-2.

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NeoTherapeutics Inc. (Nasdaq: NEOT) of Irvine, CA, said the transfer of the investigational new drug application for satraplatin has been completed.

The transfer of the IND from Bristol Myers-Squibb to NeoOncoRx, the NeoTherapeutics anti-cancer subsidiary, and will seek FDA protocol approval for a phase III trial in prostate cancer to begin later in the year.

Satraplatin is a third generation, orally administered platinum compound developed jointly by Johnson Matthey and Bristol Myers-Squibb, the company said. Satraplatin is a platinum derivative, similar to cisplatin and carboplatin, two other platinum anti-cancer drugs that Johnson Matthey helped to develop and which they manufacture. NeoOncoRx acquired the worldwide rights to develop and market satraplatin in 2001.

In another development, NeoTherapeutics Inc. said **NeoOncoRx**, its oncology division, has begun two phase II double-blind, 50-patient each, placebo-controlled studies of Neotrofin for chemotherapy-induced neuropathy.

The study will evaluate the efficacy of the drug in treating neuropathy in cancer; the revention study will look at the ability to prevent the occurrence of neuropathy for ovarian cancer treated with paclitaxel and carboplatin, the company said.

In each study patients will receive 1,000 mg of Neotrofin or placebo twice a day for 12 weeks, the company said. One-half will receive Neotrofin and

one-half will receive placebo. After 12 weeks, all patients who have continued to undergo chemotherapy or still have evidence of neuropathy will receive 1,000 mg of Neotrofin twice a day for 12 weeks.

Oncology Management:

Univ. Of Pittsburgh Plans Molecular Medicine Institute

University of Pittsburgh School of Medicine said it has partnered with **UPMC Health System** to develop the Molecular Medicine Institute to study genetic disease.

The goal of MMI will be to develop multidisciplinary pre-clinical and clinical research programs for molecular therapies, including gene transfer technologies and protein therapeutic methods.

MMI will study animal models of human disease to investigate new gene and protein transfer methods, and measure their expression and their potential for human therapy. UPMC Health System said it would provide many of the resources necessary, such as vector development and manufacturing capabilities, a vast patient base, funding, and professional support.

"Molecular medicine has provided us with seemingly unlimited possibilities for the development of new therapies," said Arthur Levine, senior vice chancellor for health sciences and dean of the University of Pittsburgh School of Medicine. "As we begin to map the human proteome, we will enter a new era in medical practice. The establishment of the University of Pittsburgh Molecular Medicine Institute will ensure our position as a leader in molecular medicine."

Joseph Glorioso, the William S. McEllory Professor of biochemistry and chairman of molecular genetics and biochemistry at UPSM, will direct MMI.

In addition to Glorioso, University of Pittsburgh researchers include: Timothy Billiar, deputy director, George Foster, professor of surgery and chairman of the department of surgery, School of Medicine, Paul Robbins, research director, professor of molecular genetics and biochemistry, School of Medicine; and John Barranger, medical director, professor, department of human genetics, Graduate School of Public Health.

In addition to support from the University of Pittsburgh and UPMC Health System, funding for the MMI will come from pre-existing federal grants including the General Clinical Research Center, grants received through the Program of Excellence in Gene Therapy, grants from foundations including the Juvenile Diabetes Research Foundation, and grants from pharmaceutical and biotechnology companies, UPSM said.

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Association of Community Cancer Centers of Rockville, MD, said it has launched a public policy Web site dedicated to regulatory and legislative issues affecting cancer patients.

The site is: http://www.accc-cancer.org/publicpolicy.

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Endocare Inc. (Nasdaq: ENDO) of Irvine, CA, it has entered into a strategic partnership with **Prostate Treatment Centers Inc**. of Spokane, WA, to develop regional cryosurgical Centers of Excellence throughout the U.S. and Canada.

Under the agreement, Endocare said it would provide each of the centers with in-office FastPSA testing equipment and its Cryocare System along with training, certification, clinical support, billing assistance to hospitals and contracting/collecting support for private insurance.

PTCI said it would provide technical support for the centers along with startup and operational oversight. PTCI will also coordinate training, proctoring and marketing as well as participate in the ownership of the Cryocare Systems.

In another development, Endocare Inc. said it has formed a strategic partnership with privately-held **Bay Area Mobile Medical LLC**, of San Francisco to form 10 regional cryosurgical centers of excellence to be called the New England Cryosurgical Alliance and be located in Maine, Vermont, New Hampshire, Massachusetts, Rhode Island and Connecticut.

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Landacorp Inc. (Nasdaq: LCOR) of Atlanta said it has reached an agreement with **M.D. Anderson Cancer Center** to implement its maxMC medical management software and e-maxMC, its web-enabling companion application, at the M.D. Anderson Physicians Network.

The agreement will allow the network to automate health plan processes including member eligibility, authorizations, tracking of care plans and enhanced coordination and communication with the cancer center, the company said.

The Landacorp maxMC software supports intricate processes, including case management and disease management.

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