THE CANCER LETTER

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House Report Offers Encouragement, But Little Else, For NCI's 2015 Plan

By Paul Goldberg

Giving NCI one of the lowest raises in recent history, the House last week offered encouragement for some of Institute Director Andrew von Eschenbach's costliest programs and applauded his goal to end "suffering and death due to cancer" 10 years from now.

"The committee commends NCI for its goal of eliminating the suffering and death caused by cancer by the year 2015," said the report that accompanied the appropriations bill passed by the House June 24. "The committee encourages NCI to pursue the use of advanced technologies such as nanotechnology, proteomics, and imaging, to rapidly translate basic research discoveries into targeted interventions to ultimately achieve the 2015 goal."

The House approved a $142,290,000 (0.5 percent) increase for NIH. This funding level is $3 million below the President's budget proposal. After the increase, the NIH budget would be $28,506,805,000.

NCI would receive a $16.5 million (0.3 percent) increase, which would

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National Cancer Policy Forum Succeeds Policy Board, IOM Appoints 22 Members

The Institute of Medicine appointed 22 members to the new National Cancer Policy Forum, established to succeed the National Cancer Policy Board.

"IOM forums are designed to allow government, industry, academic, and other representatives to meet, confer, and plan privately on subject areas of mutual interest," according to a statement by the forum. "The forum will be the successor to the board in providing a focus within the National Academies for the consideration of issues in science, clinical medicine, public health, and public policy relevant to the goals of preventing, palliating, and curing cancer."

During its eight years, from 1996 to 2004, the board identified emerging policy issues and conducted studies to bring these issues into focus and make recommendations for policy-makers. The board was funded primarily by NCI and the Centers for Disease Control and Prevention.

As a forum rather than a board, the sponsors will have full membership in the forum. Governmental sponsors of the forum include NCI, CDC, CMS, AHRQ, FDA, and HRSA. Non-governmental sponsors include the American

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House Report Endorses "Cancer Biobank," caBIG

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boost its budget to $4,841,774,000.

The House report encouraged NCI to establish a central "cancer biobank," apparently echoing von Eschenbach's past plans to launch a multibillion-dollar National Biospecimen Network. NCI-funded clinical trials cooperative groups viewed the NBN initiative as a threat to their ability to continue collection of tissues and maintain libraries of annotated tissues from trials conducted over past decades.

"The committee believes that the cancer biobank, because it will centralize and standardize molecular annotation of tissues, has the potential to greatly accelerate the understanding of cancer and the discovery and development of new biomarkers, new diagnostics and new therapeutic approaches," the report said. "As it is established by NCI, the committee believes that it will be most efficient to utilize existing technologies such as high-density microarrays, given the long time frame for the development of new technologies."

The cancer Biomedical Informatics Grid (caBIG), too, received a boost from the committee.

"The committee is pleased with NCI's development of [caBIG] as a network to facilitate the integration of diverse data types and the sharing of interoperable analytic tools. NCI is encouraged to work with the Office of the National Coordinator for Health Information Technology to use caBIG as a prototype for an interoperable clinical data network," the document states.

Lobbyists routinely influence the language of appropriations reports, allowing bureaucrats and private interests to demonstrate that they have supporters in Congress. For legislators, report language provides an opportunity to be more generous with bestowing mandates than with actual appropriations.

Despite its enormity, von Eschenbach's pledge to turn cancer into a chronic disease hasn't echoed within the Administration. The NCI director unveiled the plan in a speech two and a half years ago (The Cancer Letter, Feb. 14, 2003).

NIH Director Elias Zerhouni has maintained a long, conspicuous silence on the subject. In his first public comment, last month, the NIH director established a boundary, stressing that the goal is wholly von Eschenbach's, and that its purpose is to galvanize the field through symbolism.

"All goals are goals: something you strive for," Zerhouni said in an interview published in the June 3 issue of Science. "And I think [NCI] firmly believes that this is a way to energize their field, to really go toward a—not eliminating cancer, but making cancer a chronic disease. That's what Dr. von Eschenbach will tell you. That's really what the idea of doing that is, to sort of project the need for a measurable endpoint."

In a recent lecture, Harold Varmus, Zerhouni's predecessor at NIH, challenged von Eschenbach's goal. "We have a long way to go before we beat cancer," Varmus said at the annual meeting of the American Society of Clinical Oncology (The Cancer Letter, May 20). "We are not going to do so before 2015."

Meanwhile, von Eschenbach has come up with an even more optimistic plan. Responding to questions from Sen. Arlen Specter (R-Penn.) at a hearing this spring, the Institute director said that with additional appropriations of $600 million a year, suffering and death from cancer could be halted by 2010 (The Cancer Letter, May 20).

Von Eschenbach was working on a document outlining the 2010 plan. However, the document had to be cleared by NIH and HHS officials.

"Sen. Specter specifically asked for an updated report on increasing the nation's investment to try to increase the pace of progress for eliminating the suffering and death due to cancer," von Eschenbach said to the NCI Board of Scientific Advisors June 27. "That process is ongoing."

THE CANCER LETTER

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House Bill "De-funds" Peer-Reviewed Projects

The House appropriations bill includes an amendment that strips funding from two grants that have gone through peer review and received funding. Rep. Randy Neugebauer (R-Tex.) introduced the amendment to withhold funds from two National Institute of Mental Health grants.

One of the projects, titled "Perceived Regard and Relationship Resilience," follows newlyweds. In it's fifth year, the grant is slated to receive $345,161. Another study, "Perceptual Bases of Visual Concepts," examines the ability of pigeons to process information. The study received about $1.5 million over 15 years.

In a statement, Neugebauer said the studies were irrelevant to the NIMH mission. "If all of the NIMH funds being spent on research on happiness had instead been spent developing better treatment for depression, there would be a lot more happy people than just the NIMH grantees," he said.

Conceding that "some bird research has generated interesting research results," Neugebauer said that "it is difficult to imagine what useful information could be derived that would have any value for understanding mental illness."

The amendment was accepted "en bloc," without discussion, on the House floor June 24.

"De-funding meritorious grants on the floor of Congress is unjustified scientific censorship," NIH Director Elias Zerhouni said in a statement. "It undermines the historical strength of American science which is based on our world-renowned, apolitical, and transparent peer review process."

Members of the NCI Board of Scientific Advisors said they were concerned about Congress second-guessing peer review. "While these happen not to be cancer-related grants, I suspect that for many of us, this notion of de-funding existing grants that were reviewed and approved by peer review is a very chilling event," Board Chairman Robert Young, president of Fox Chase Cancer Center, said at the board meeting June 27.

It is unlikely that a similar amendment would appear in the Senate bill, or that the measure would survive in conference, when the House and Senate bills are reconciled, Capitol Hill observers said.

The text of the House report follows:

National Cancer Institute: The committee provides $4,841,774,000 for the National Cancer Institute, which is $16,515,000 above the fiscal year 2005 comparable level and the same as the budget request. The bill includes language requested by the Administration permitting up to $8,000,000 for repairs and improvements to the NCI intramural facility in Frederick, Md.

Mission—The NCI conducts and supports basic and applied cancer research in early detection, diagnosis, prevention, treatment and rehabilitation. NCI provides training support for research scientists, clinicians and educators, and maintains a national network of cancer centers, clinical cooperative groups, and community clinical oncology programs, along with cancer prevention and control initiatives and outreach programs to rapidly translate basic research findings into clinical practice.

Prostate Cancer—The committee recognizes NCI's commitment to prostate cancer research as laid forth in its Prostate Cancer Research Plan, FY 2003-FY 2008. The committee requests that NCI provide an annual update every January on its progress in prostate cancer research as it reflects the goals outlined in the plan for years fiscal years 2006-08. In developing this update, the committee urges the NIH to consult and work closely with the research community, clinicians, and patient advocacy groups and the Congress.

Breast cancer—Breast cancer's toll continues to threaten the lives and the quality of life of thousands of women. In addition to ongoing research activities underway at the Institute, the committee hope that increased attention will also be given to areas of research that focus on helping women to more fully restore and improve their quality of life after treatment, including further research on lymphadema, stress, nutrition, exercise, weight, and environment.

The committee remains concerned about missed opportunities in breast cancer screening, detection, prevention, control, early diagnosis, and mammogram detection, reading and analysis. The committee encourages NCI to further accelerate advances in breast cancer screening technology and to capitalize on existing and create new technologies that improve early diagnosis, health outcomes, and survival.

Ovarian cancer—The committee remains concerned that survival rates associated with ovarian cancer have improved only slightly over the past 20 years. Ovarian cancer is the deadliest of all gynecological cancers. For all women diagnosed with ovarian cancer, the five-year survival rate is 45 percent. More than two-thirds of the women have advanced disease at the time of diagnosis, and for this group, the 5-year survival rate is 29 percent. The committee commends NCI for its recognition of the importance of studying this deadly women's disease and appreciates the NCI's recent investment that is helping to increase

the understanding of the unique molecular pathways associated with ovarian cancer through its SPOREs program. The committee encourages NCI to sustain and strengthen its commitment to and investment in ovarian cancer and maintain the specialized programs of research excellence initiatives directed toward ovarian cancer in fiscal year 2006.

Liver Cancer—The committee remains concerned with the increasing incidence of primary liver cancer, which is in sharp contrast to many other forms of cancer where the incidence is declining and the treatment options are rapidly increasing. The committee is aware that NCI, working with NIDDK, has convened an Experts Conference and is moving ahead with plans to increase resources dedicated to this disease. The committee urges NCI to make a strong commitment to research on primary liver cancer with particular focus on the development of drugs that target the cancer without killing healthy cells by interfering with the cellular pathways of the disease. The committee further urges NCI to continue to support the NIDDK sponsored HALT-C clinical trial which has particular relevance to the NCI mission.

Pancreatic cancer—Pancreatic cancer is the country's fourth leading cause of cancer death. Most patients present with advanced disease at diagnosis and the median overall survival rate for people diagnosed with metastatic disease is only about six months. The committee is concerned that there are too few scientists researching pancreatic cancer and compliments the NCI's past efforts for increasing the research field through its program of a 50 percent formalized extended payline for grants that were 100 percent relevant to pancreatic cancer. The committee considers this an important method for attracting both young and experienced investigators to develop careers in pancreatic cancer. In 2004, the NCI established a new policy for awarding additional grants in pancreatic cancer research and extended this initiative to research that is 50 percent relevant to pancreatic cancer. The committee requests NCI to report in February, 2006 on how the two changes in policy have affected the pancreatic cancer portfolio, including the percentage relevancy of each grant to pancreatic cancer, and urges NCI to continue its commitment to fertilize the pancreatic cancer field.

Lymphoma—Lymphoma is the fifth most common cancer and the most common hematological cancer. Unlike many other cancers, lymphoma often strikes individuals in young adulthood and the middle years, significantly impacting their professional productivity and individual role in the family and society. The committee recommends that NCI take bold action to address lymphoma as a public health problem and to capitalize on important research advances to date. The committee encourages NCI to strengthen its investment in translational and clinical lymphoma research.

The committee commends NCI and the National Institute of Environmental Health Sciences for convening a workshop on the viral and environmental links to lymphoma and recommends that steps be taken to strengthen the NCI investment in this area. The committee recommends that NCI direct resources to: (1) studies of adequate scope to assure the identification of environmental risk factors for specific subtypes of lymphoma; (2) small studies designed to improve detection and quantification of historically difficult-to-measure environmental factors; (3) studies that are directed toward enhancing the understanding of the role of the immune system in the initiation and progression of lymphoma; and (4) studies that examine the simultaneous presence of a wide profile of infectious agents among individuals with lymphoma.

The committee recommends that resources be directed to research related to long-term survivors of both non-Hodgkin's lymphoma and Hodgkin's lymphoma. The report of the Leukemia, Lymphoma, and Myeloma Progress Review Group (LLM PRG) recommended that resources be invested in identifying the populations of patients that are at high risk of adverse outcomes from their treatment for lymphoma.

Cancer centers at minority institutions—The committee commends NCI on the success of its cancer centers program. Given that minority populations suffer disproportionately from virtually every form of cancer, the committee encourages NCI to give consideration to supporting the establishment of a comprehensive center at a minority institution focused on research, treatment, and prevention of cancer in African American and other minority communities. The committee is pleased with NCI's attention to this important matter.

Neurofibromatosis—The committee is pleased with NCI's clinical trials of NF patients and encourages NCI to enhance its NF research portfolio in such areas as further development of animal models, natural history studies, therapeutic experimentation, and clinical trials. The committee recognizes that basic research has successfully brought NF into the clinical era and encourages NCI to create, fund, and implement NF clinical trial infrastructures including NF centers, patient data bases, and tissue banks. The committee further encourages NCI to apply existing cancer drugs to NF patients in clinical trials and to develop new drugs for

NF, which could then apply to the general population because of NF's connection to many forms of human cancer. The committee is aware of significant new advances in NF research in the past few years in the area of tumor suppression and encourages NCI to continue to coordinate its efforts with other NIH institutes and government agencies.

Angiogenesis—The committee applauds NCI, working with other Institutes, for its leadership in planning and launching the Trans-NIH Angiogenesis Research Program (TARP) that promotes multidisciplinary research on the control and promotion of new blood vessel growth. This research has the potential to lead to the development of new therapeutic strategies for a variety of diseases, including cancer, diabetic eye disease, diabetic kidney disease, and others.

Hemophilia—The committee understands that field work on the Multi-Center Hemophilia Cohort Study will be complete in September, 2005. This cohort offers a rich database for improving the understanding of hepatitis C virus and other concerns of major public health interest. The committee expects NCI to take all necessary steps to ensure the samples obtained through this cohort are preserved and accessible for future research. The committee also requests a report by March 31, 2006 on possible future research opportunities using the cohort samples.

Tuberous sclerosis complex—TSC is a genetic disorder that triggers uncontrollable tumor growth in multiple organs of the body, including the brain, heart, kidneys, lungs, liver, eyes or skin. In light of its similarities to the uncontrolled growth of cancer cells, many scientists believe that determining the cause of tumor growth in TSC could open the way for cures and treatments for cancer as well. To those ends, the committee strongly encourages NCI to support programs examining the molecular and cellular basis of TSC, and the role of TSC in tumor development.

American Russian Cancer Alliance—The committee applauds the progress of ARCA in harnessing the scientific strengths of its partners in pursuit of novel research activities that ultimately benefit cancer patients worldwide. The committee notes in particular the continued development of the unique ARCA projects in molecular imaging and radioisotope-targeted therapy that have strengthened the scientific collaborations with the leading Russian nuclear research centers and American cancer centers. Moreover, the committee recognizes and commends NCI for providing support to the ARCA infrastructure and facilitating international exchange and communication between the American and Russian partners. The committee encourages NCI to continue and enhance its support for the research programs of ARCA, recognizing both the scientific opportunities within the partnership and the national interest in fostering the international effort to develop new, productive avenues for the use of nuclear stockpiles previously earmarked for weapons development.

Cancer metastasis—The NCI is encouraged to develop an interdisciplinary and integrated approach to study bone metastasis, by combining the expertise of oncologists, bone biologists and metastasis experts. Key issues to address include the generation of novel organ-like or mouse models which closely mimic tumor bone interactions that will pave the way for delineating novel mechanisms of how tumor cells go to the bone; designing novel targets for better prognosis; and effective therapeutic targeting. The committee encourages NCI to continue supporting research that furthers the understanding of the causes and consequences of sarcoma. The committee also recommends that NCI support research on osteosarcoma to improve survival and quality of life and to prevent metastatic osteosarcoma in children and teenagers who develop this cancer.

Tobacco harm reduction—The committee recognizes and applauds the significant work of HHS and its agencies in the area of tobacco and health, particularly recent efforts aimed at facilitating smoking cessation. The committee believes it is important to continue to explore additional methods to reduce smoking related mortality and morbidity in the 10 to 15 percent of the adult population who cannot or will not quit smoking. In a recent study funded by NCI, a panel of leading tobacco experts was asked to review scientific literature for the comparative mortality risks of low-nitrosamine smokeless tobacco products and conventional cigarettes. The panel of experts concluded that, based on published scientific literature, low-nitrosamine smokeless tobacco products pose a substantially lower risk to the user than conventional cigarettes. Given this important conclusion, the committee urges NCI to continue its research into harm reduction strategies for cigarette smokers, and consider the role low-nitrosamine smokeless tobacco products may play in the overall effort to reduce the incidence of cigarette smoking in the U.S.

Cancer biobank—The committee believes that the cancer biobank, because it will centralize and standardize molecular annotation of tissues, has the potential to greatly accelerate the understanding of cancer and the discovery and development of new biomarkers, new diagnostics and new therapeutic approaches. As it is

established by NCI, the committee believes that it will be most efficient to utilize existing technologies such as high-density microarrays, given the long time frame for the development of new technologies.

Advanced technologies—The committee commends NCI for its goal of eliminating the suffering and death caused by cancer by the year 2015. The committee encourages NCI to pursue the use of advanced technologies such as nanotechnology, proteomics, and imaging, to rapidly translate basic research discoveries into targeted interventions to ultimately achieve the 2015 goal.

Informatics grid—The committee is pleased with NCI's development of the cancer Biomedical Informatics Grid (caBIG) as a network to facilitate the integration of diverse data types and the sharing of interoperable analytic tools. NCI is encouraged to work with the Office of the National Coordinator for Health Information Technology to use caBIG as a prototype for an interoperable clinical data network.

National Institutes of Health: The committee provides $28,506,805,000 for the 26 appropriations which together fund the programs of the National Institutes of Health. The total in the bill is $142,290,000 above the fiscal year 2005 comparable level and $2,979,000 below the budget request. This amount includes $97,021,000 for targeted research activities to develop radiological, nuclear and chemical threat countermeasures. The Administration had requested this funding in the Public Health Social Services Emergency Fund.

Roadmap—The committee endorses the Administration's proposal of supporting the NIH Roadmap for Biomedical Research at a funding level of $332,800,000 from funding contributed by the Institutes and Centers based on less than one percent of their budgets and out of the Director's Discretionary Fund. The committee believes the Roadmap is an important step to moving biomedical research forward to the next level of discovery at a pace that hastens its delivery to patients. The Roadmap addresses common needs across all disease areas and should produce research advances that will benefit many diseases and conditions. The committee expects to be notified on a quarterly basis if the contribution from the Institutes and Centers or the allocation of funding by initiative changes from what is presented in the congressional justification.

Biodefense—The Administration's fiscal year 2006 budget for NIH includes $1,791,000,000 for bioterrorism activities, including funds proposed in the Public Health and Social Services Emergency Fund. The committee has included the $97,021,000 requested for NIH within the Emergency Fund directly in the NIH Office of the Director appropriation. The committee has not identified a specific funding level for biodefense research, choosing to give the Director of NIH flexibility in determining what share of NIH resources should be considered biodefense activities.

Balance in the research portfolio—The committee reiterates its longstanding view that NIH should distribute funding on the basis of scientific opportunity. The committee urges the Director and the Administration to continue to resist pressures to earmark, set aside and otherwise politicize these resources. To enhance NIH's flexibility to allocate funding based on scientific opportunity, the committee has attempted to minimize the amount of direction provided in the report accompanying the bill. For example, there are no directives to fund particular research mechanisms, such as centers or requests for applications, or specific amounts of funding for particular diseases.

In stating that scientific opportunity should be the basis for allocating research funding, the committee understands that other factors also are relevant to NIH's decisions, including such considerations as the infectious nature of a disease, the number of cases and deaths associated with a particular disease, the Federal and other costs of treating a disease, the years of productive life lost due to a particular disease, and the estimated proximity to research breakthroughs. The committee does not presume to judge which criteria should take precedence or carry the greatest weight in individual funding decisions, but urges NIH to consider the full array of relevant criteria as it constructs its research portfolio. The committee applauds the Director's focus on the need to address chronic diseases with preemptive interventions before symptoms appear and function is lost.

AIDS funding—Consistent with the philosophy outlined above, the committee has chosen not to earmark a specific dollar amount for AIDS research. The committee understands that it would be NIH's intent to allocate AIDS funding consistent with the Director's recommendations. The committee understands that this allocation may change before the beginning of the fiscal year.

The committee intends that the funds allocated for AIDS should be spent in a manner fully consistent with the AIDS research plan developed by the Office of AIDS Research and expects the Director of NIH to use the full authority of his office to ensure that this occurs. The committee has provided the Director of

OAR, jointly with the Director of NIH, transfer authority to reallocate up to three percent of funds designated for AIDS research among Institutes, subject to normal reprogramming procedures. The committee encourages NIH to use this authority whenever it believes that an adjustment in the allocation of AIDS funding between Institutes is appropriate to achieve scientific objectives or to facilitate promising research efforts.

The committee continues to support OAR, its leadership, and its coordinated budget planning process and expects the individual institutes and centers to fully cooperate with OAR's work. The committee has provided funding for the OAR within the Office of the Director and intends that the OAR will maintain its current structure and responsibilities, including the allocation of an emergency discretionary fund.

NCI Programs:

NCI To Commit $7 Million To Clinical Trials Restructuring

By Kirsten Boyd Goldberg

NCI will commit $7 million this year to begin the restructuring of its cancer clinical trials system as outlined in a report of the Clinical Trials Working Group, Institute Director Andrew von Eschenbach said to the NCI Board of Scientific Advisors at its June 27 meeting.

The report, accepted by the National Cancer Advisory Board earlier this month, made 22 recommendations for strengthening the clinical trials system, including establishing new peer review panels for developing and prioritizing phase III clinical trials concepts (The Cancer Letter, June 10).

Von Eschenbach praised the five-year, $113-million plan as "a very extensive, comprehensive, and insightful report… that will require even reorganization with the NCI itself with regard to how we go about administering and managing the clinical trials process."

NCI will begin restructuring "immediately, with a very rapid implementation phase that's intended to be what we euphemistically are referring to as design-build," von Eschenbach said. "We have laid the foundation and are in the process of building, but at the same time recognizing that there may be ongoing modification that will be necessary by virtue of what we learn and what we experience. It is not a blueprint of a plan that is absolutely final, but it is a blueprint of a plan that we are implementing."

The recommended changes will enable NCI to hasten progress in cancer research, von Eschenbach said. "The Clinical Trials Working Group report, and now its implementation, is one of our important components to a constant acceleration of our forward trajectory of progress as we move towards eliminating the suffering and death due to cancer," he said.

The report is available at http://integratedtrials.nci.nih.gov/.

* * *

PROTEOMICS: The board unanimously approved NCI's plan to set aside $104 million over five years to fund grants and contracts to advance the field of cancer proteomics.

The Clinical Proteomics Technologies Initiative would seek applicants for seven to 10 R01 grants, five to seven R21/R33 grants, and five U24 research and development contracts.

A full report on the initiative is scheduled for publication in the July 8 issue of The Cancer Letter.

* * *

ACCELERATION: Cancer research is moving faster than ever before, von Eschenbach said in his Director's Report to the Board of Scientific Advisors.

"The journey to 2015 continues," von Eschenbach said. "What we are continuously appreciating is that the pace of progress is continuing to accelerate.

"When we began three and a half years ago, we really began with the expectation that there was a goal, a proximate destination that we had set for ourselves, to eliminate the suffering and death due to cancer, and, in many ways, the road to that goal was really quite obscure," he said. "But what was not obscure was where we had come from. When we looked back at the trajectory of progress, it seemed that we were, in fact, at a very special moment in time, where we would move from traditional macroscopic or microscopic appreciation of cancer, to now one that was, in fact, molecular."

Now that "the new reality" of molecular appreciation of cancer is in place, "it's important to maintain the focus on our goal," von Eschenbach said.

* * *

DECELERATION: Four advisors completed their terms on the Board of Scientific Advisors earlier this week: **Neil Clendeninn**, of Clinical Pharmaceutical Consulting; **Thomas Curran**, of St. Jude Children's Research Hospital; **William Kaelin**, of Dana-Farber Cancer Institute; and **Christine Miaskowski**, of University of California, San Francisco.

"There certainly is a sense of fear and trepidation in the community" regarding NCI funding for research grants, Curran said in brief remarks to the board. "How you deal with it and how you keep things moving ahead,

I don't have the answer…. I hope that by working together with [NCI Director] Andy [von Eschenbach] and NCI, you will come up with a stronger and better NCI in the future that will serve the needs of all the populations of patients as well as scientists."

Funding Opportunities:

Program Announcement

PA-05-125: Diet-Induced Changes in Inflammation as Determinants of Colon Cancer. The goals of the initiative are to: 1) identify and characterize diet-induced changes in anti- and pro-inflammatory mediators that modulate colon cancer risk; 2) define genetic polymorphisms that modify the response to specific bioactive food components with regard to colon cancer inhibition; and 3) unravel the physiological effectiveness of dietary components in terms of concentration, activity, duration of exposure, degree of stability, chemical forms, and binding affinity to receptors in inflammatory colonocytes. Investigators may choose from the full range of preclinical or clinical approaches. The focus should be on defining the physiological significance of diet in modulating inflammatory processes that may be linked to colon cancer development. Since inflammatory processes can also be influenced by post-translational mechanisms (e.g., protein-protein interactions, modification of protein activities through acetylation, phosphorylation, and methylation, degradation by the ubiquitin-proteasome mediated pathway), the profiling of proteins and/or metabolites in cells or tissues should provide greater insight into the relevance of dietary treatments to inflammatory processes on colon cancer.

The efficient utilization of molecular resources such as gene, protein, and metabolome databases may be used to expedite research. Bioinformatic approaches may also be necessary to identify patterns of gene, protein, and/or metabolite changes that can generate unique fingerprints for the given dietary treatments. The PA seeks applications for R01 and R21 grants. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-05-125.html.

Inquiries: Scientific/Research Contacts: Young Kim, NCI Division of Cancer Prevention, phone 301-496-0126, e-mail yk47s@nih.gov.

RFP Available

N02-CP-41016-50: Interdisciplinary Studies of Genetic and Environmental Causes of Cancer. NCI Genetic Epidemiology Branch is re-competing a contract for support for interdisciplinary studies currently held by Westat Inc. The contract will establish a mechanism to provide all the services required for domestic and international family studies and field (case-control and cohort) studies. The RFP may be accessed via the NCI Research Contract Branch Web site at http://rcb.cancer.gov/rcb-internet/.

Inquiries: Karen McFarlane, contracting officer, phone 301-435-3782; fax 301-480-0241.

NCI-FDA Fellowship Program

NCI and FDA seek applicants for the first federal government program that encompasses the development and regulation of new medical products.

The program will train a cadre of scientists in cancer research and research-related regulatory review to develop skill sets that bridge the two distinct processes. Eligible candidates must have an M.D. and/or Ph.D. or an equivalent degree and must also be either a citizen of the U. S. or have permanent residency status.

For further information, see http://iotftraining.nci.nih.gov.

IOM Names 22 To Policy Forum

(Continued from page 1)

Cancer Society, the American Society of Clinical Oncology, C-Change, and UnitedHealth Group. Besides the sponsor representatives, the forum will include 12 members from academia, cancer care, pharmaceutical industry, and patient advocacy.

Harold Moses, director emeritus of the Vanderbilt-Ingram Cancer Center, is chairman of the forum.

Members include: Edward Benz, president, Dana-Farber Cancer Institute; Kevin Brady, acting director, CDC Division of Cancer Prevention and Control; Thomas Burish, ACS board chairman, and president, Washington and Lee University; Mark Clanton, NCI deputy director for cancer delivery systems; Connie Curran, executive director, C-Change; Joseph Fraumeni Jr., director, NCI Division of Cancer Epidemiology and Genetics; Betty Ferrell, research scientist, City of Hope National Medical Center; Stephen Friend, executive vice president for oncology, Merck; Patricia Ganz, ASCO board member and professor of medicine, University of California, Los Angeles; William Lawrence, director, AHRQ Center for Outcomes and Evidence; Lynn Matrisian, chairman, Division of Cancer Biology, Vanderbilt; William McGuire, chairman and CEO, UnitedHealth Group; David Parkinson, vice president oncology, Amgen; Edith Perez, director, Cancer Clinical Study Unit, Mayo Clinic; Scott Ramsey, associate member, Fred Hutchison Cancer Research Center; William Robinson, director, HRSA Office of Minority Health and Health Disparities; Charles Sawyers, professor of hematology/oncology, UCLA; Margaret Spitz, chairman of epidemiology, M.D. Anderson Cancer Center; Ellen Stovall, president and CEO, National Coalition for Cancer Survivorship; Sean Tunis, chief medical officer, CMS (alternate, Peter Bach, senior advisor to the administrator, CMS); and Janet Woodcock, FDA acting deputy commissioner for operations.

A Notch-Signaling Pathway Inhibitor in Patients with T-cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL)

An investigational study for children, adolescents and adults with relapsed and refractory T-cell acute lymphoblastic leukemia/lymphoma is now accruing patients at various centers around the country.

This study's goal is to evaluate the safety and tolerability of a Notch inhibitor as a rational molecular therapeutic target in T-ALL, potentially uncovering a novel treatment for these cancer patients.

Eligibility criteria and treatment schema for the study include:

Notch-Signaling Pathway Inhibitor in Patients with T-ALL	
Eligibility Criteria	Patient must be = 12 months with a diagnosis of T-cell acute lymphoblastic leukemia/lymphoma AND must also have: • Relapsed T-ALL • T-ALL refractory to standard therapy • Not be a candidate for myelosuppressive chemotherapy due to age or comorbid disease ECOG performance status =2 for patients >16 years of age OR Lanksy performance level >50 for patients 12 months to =16 years of age Fully recovered from any chemotherapy and >2 weeks from radiotherapy, immunotherapy, or systemic steroid therapy with the exception of hydroxyurea or intrathecal therapy Patient must be >2 months following bone marrow or peripheral blood stem cell transplantation No treatment with any investigational therapy during the preceding 30 days No active or uncontrolled infection
Treatment Plan	Open label and non-randomized, this study is conducted in two parts. Part I is an accelerated dose escalation to determine the maximum tolerated dose (MTD), and Part II is a cohort expansion at or below the MTD. MK-0752 will be administered orally. Plasma concentrations will be measured at defined time intervals.

For information regarding centers currently open for enrollment, please contact 1-888-577-8839.

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THE CANCER LETTER

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Business & Regulatory Report

Oncology Management:

CMS Competitive Acquisition Program To Buy Part B Drugs For Physicians

The Centers for Medicare & Medicaid Services issued an interim final rule to establish a competitive acquisition program that would serve physicians who administer drugs in their offices.

The program is slated to open Jan. 1. Physicians who choose to take part in the program will be able to obtain drugs from vendors selected by Medicare through competitive contracting.

Physicians would bill Medicare only for the service of administering the drugs, the agency said. The vendors would bill the federal program for the drugs, and will be responsible for collecting deductibles and coinsurance on

(Continued to page 2)

Product Regulation:

FDA Approves Xeloda For Adjuvant Treatment Of Colorectal Cancer

FDA approved Xeloda (capecitabine) for the adjuvant treatment of colon cancer.

"Following European approval in March 2005 the FDA also supports Xeloda's new indication," said William Burns, head of the pharmaceuticals division of **Roche Pharma**. "For the first time, colon cancer patients will have access to a unique treatment option that provides an effective oral therapy which is well-tolerated and can be taken at home."

The FDA's decision was based on the X-ACT (Xeloda in Adjuvant Colon Cancer Therapy) trial. The trial met its primary endpoint, showing Xeloda is non-inferior to 5-FU/LV for disease-free survival, the company said. At this time, neither Xeloda nor combination chemotherapy has been shown to prolong overall survival. Combination chemotherapy has demonstrated an improvement in disease-free survival compared to 5-FU/LV.

"It provides a safe, effective, alternative means offering patients the opportunity to receive pill therapy in the comfort of their home rather than needing to come into the clinic for repeated IV injections," said Howard Burris, of the Sarah Cannon Research Institute in Nashville.

On average, a patient needed eight hospital visits when treated with Xeloda, compared to 30 visits if treated with intravenous 5-FU/LV. Xeloda is an oral fluoropyrimidine.

Xeloda in combination with docetaxel is indicated for metastatic breast cancer after failure of prior anthracyline-containing chemotherapy. Xeloda monotherapy is also indicated for metastatic breast cancer resistant

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Acquisition Program Includes 181 Drugs Paid By Part B

(Continued from page 1)

the drugs from the beneficiary or a third party insurer.

"This new competitive approach for Part B drugs aims to give physicians a new and less burdensome option for acquiring the treatments their patients need," CMS Administrator Mark McClellan said in a statement. "The program frees physicians from the administrative work of purchasing and procuring drugs in their offices, so that they can focus more time and resources on providing the best treatments for their patients."

Of approximately 440 drugs that are billed incident to a physician service and paid under Part B, 181 will be included in the CAP, accounting for 85 percent of all Medicare spending on physician injectable drugs, the agency said.

Physicians who choose not to participate would continue to purchase drugs directly from drug suppliers and be paid directly by Medicare at the rate of 106 percent of the manufacturers' average sales price, the agency said.

"This is an innovative approach to using competition to reduce the burden on physicians related to using drugs in their offices, and we intend to work with all key stakeholders to assure that the program provides the greatest benefits at the lowest cost," McClellan said in a statement.

Vendors wishing to participate will have to submit a bid showing the prices at which they propose to furnish the drugs included in CAP.

CMS will select winning vendors based on their bid prices and their demonstration that they meet Medicare's quality standards.

A fact sheet on the CAP program is available at www.cms.hhs.gov/media/press/release.asp?Counter=1492.

The text of the interim final rule will be published in the Federal Register on July 6.

* * *

US Oncology of Houston said it has started a pharmaceutical distribution business to serve medical oncology practices in the U.S.

"Our business will enable a seamless flow of pharmaceuticals directly from the manufacturers to the oncology practices and their cancer patients," said Bruce Broussard, executive vice president of pharmaceutical services and chief financial officer of US Oncology. "There is tremendous pressure to control healthcare costs. We believe that our distribution business will help network practices realize significant operating efficiencies and help them continue a tradition of high quality patient care."

US Oncology said it would integrate the purchasing, storage, and distribution of $1.6 billion in pharmaceuticals for the 470 sites of service of the network, thereby optimizing the pharmaceutical supply chain.

Improving waste tracking and inventory management, as well as providing operational efficiencies by decreasing paper processing would reduce costs, the company said. Buying direct from the manufacturers would ensure the integrity of the product and improve patient safety, the company said.

The pharmaceutical distribution program would begin in the fall of 2005 at its site in Fort Worth, the company said.

Product Regulation:

FDA Approves Xeloda; CHMP Recommends Tarceva

(Continued from page 1)

to both paclitaxel and an anthracycline-containing chemotherapy regimen or resistant to paclitaxel and where further anthracycline therapy is not indicated.

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Tarceva (erlotinib) received a positive recommendation from the European Committee for Medicinal Products for Human Use (CHMP) for the treatment of non-small cell lung cancer.

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The committee recommended that Tarceva should be indicated for the treatment of patients with locally advanced or metastatic non-small-cell lung cancer after failure of at least one prior chemotherapy regimen.

"This decision is proof of the impressive survival benefit that Tarceva offers patients with late stage lung cancer," said William Burns, head of the pharmaceuticals division of **Roche Pharma**. "This brings new hope to lung cancer patients who have currently very limited treatment options."

When prescribing Tarceva, factors associated with prolonged survival should be taken into account.

The CHMP recommendation is based on data from a pivotal phase III study which compared Tarceva to placebo for the treatment of patients with advanced NSCLC, following failure of first or second-line chemotherapy.

Patients receiving Tarceva lived significantly longer than those in the placebo arm. There was also a significant increase in both the length of time before patients' disease symptoms deteriorated and the time when patients were stable and there was no progression of their cancer.

It was also observed that one out of three patients on Tarceva was alive at one year as opposed to only one of five in the placebo group.

There is no specific recommendation for EGFR IHC (immunohistochemistry) testing.

Tarceva is being evaluated in clinical trials through an alliance among OSI Pharmaceuticals, Genentech, and Roche.

Chugai is pursuing its development and regulatory approval for the Japanese market.

In the U.S., Tarceva is marketed by Genentech.

* * *

DakoCytomation received FDA approval for its c-Kit pharmDx test to be used as an aid in identifying GIST positive patients eligible for treatment with Gleevec therapy.

The c-Kit pharmDx test is an immunohistochemistry assay designed to qualitatively identify c-kit protein/ CD117 antigen expression in normal and neoplastic tissues.

The test has been available in South America and Europe since August 2004.

Gleevec, marketed by Novartis, is indicated for the treatment of Kit (CD117)-positive unresectable and/or metastatic malignant GIST. It inhibits proliferation and induces apoptosis in gastrointestinal stromal tumor (GIST) cells, which express an activating c-kit mutation.

DakoCytomation is privately owned and headquartered in Denmark.

* * *

ImClone Systems Inc. (Nasdaq: IMCL) of New York said it would submit a supplemental biologics license application for Erbitux (cetuximab) in combination with radiation and as a single agent in squamous cell carcinoma of the head and neck in the third quarter of 2005.

According to the company, the following clinical trials would serve as the basis of the sBLA:

—A randomized, international phase III trial, conducted by ImClone and Merck KGaA, examining the impact of combining Erbitux with radiation on locoregional control and overall survival in 424 patients with locally advanced SCCHN.

—A multicenter phase II trial conducted by Merck evaluating the response rate of Erbitux as a single agent in 103 patients with advanced recurrent and/or metastatic SCCHN not suitable for further local therapy and who have failed platinum-based chemotherapy.

* * *

Praecis Pharmaceuticals Inc. (Nasdaq: PRCS) of Waltham, Mass., has discontinued promotional activities related to Plenaxis (abarelix for injectable suspension), a drug for advanced prostate cancer.

Plenaxis is now available only to available to those patients in the U.S. who are now receiving the drug.

"This difficult decision was prompted solely by commercial considerations, and was not prompted in any way by safety, efficacy or other regulatory issues," the company said.

Only physicians enrolled in a limited access program will be able to prescribe the drug.

"You should not utilize product in your inventory to initiate new patients on Plenaxis therapy," the company said in a letter to physicians. "Any unused kits of Plenaxis should be returned to the distributor from whom you made your purchase for a refund."

Plenaxis is indicated for the palliative treatment of men with advanced symptomatic prostate cancer, in whom LHRH agonist therapy is not appropriate and who refuse surgical castration, and have one or more of the following: (1) risk of neurological compromise due to metastases, (2) ureteral or bladder outlet obstruction due to local encroachment or metastatic disease, or (3) severe bone pain from skeletal metastases persisting on narcotic analgesia.

The drug was approved in November 2003. Its label warns about "immediate onset systemic allergic reactions."

Clinical Trials:

Curis Begins Phase I Trial In Basal Cell Carcinoma

Curis Inc. (Nasdaq: CRIS) of Cambridge, Mass., said it has begun dosing in a phase I trials for basal cell carcinoma.

The drug candidate, a topical antagonist of the Hedgehog signaling pathway, was discovered by Curis and is being co-developed through a collaboration between Curis and **Genetech** (NYSE: DNA).

The trial is a double-blind, randomized, placebo-controlled study of 66 subjects that would measure outcomes measured of safety and tolerability of a multi-dose regimen of the Hedgehog antagonist, the company said. The study will take place at ten sites in the U.S., the company said.

* * *

ImmunoGen Inc. (Nasdaq: IMGN) of Cambridge, Mass., said it has begun testing huC242-DM4, a tumor activated product compound for colorectal, pancreatic, and cancers that express the CanAg antigen targeted by the compound.

In the study, huC242-DM4 will be administered once every three weeks for refractory CanAg-expressing cancers.

The primary study objective is to evaluate the safety and pharmacokinetics of huC242-DM4 and to identify the maximum tolerated dose of the compound, the company said. Once the MTD is defined, additional patients will be enrolled with tumors that consistently and intensely express CanAg.

An earlier version of huC242-DM4, cantuzumab mertansine, was found to be well tolerated at doses that evidenced biological activity, the company said. In preclinical studies, huC242-DM4 was more active than cantuzumab mertansine with comparable tolerability.

Anthony Tolcher is the principal investigator for the phase I dose-escalation study underway at the Cancer Therapy and Research Center in San Antonio, Tex.

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Merck & Co. Inc. (NYSE: MRK) of Whitehouse Station, N.J., and **Vertex Pharmaceuticals Inc**. (Nasdaq: VRTX) of Cambridge, Mass., said they have begun a third phase I study of VX-680, a small molecule inhibitor of Aurora kinases.

The two-part, open-label, dose escalation study is designed to evaluate the safety and tolerability of VX-680 when administered over a five-day treatment cycle for hematologic cancers, the companies said.

The study will evaluate the agent for relapsed or refractory acute myelogenous leukemia, myelodysplastic syndrome, acute lymphocytic leukemia or chronic myelogenous leukemia in blast crisis, the companies said.

VX-680 is an inhibitor of Aurora kinases and of Flt-3 kinase, the companies said. The inhibitor has demonstrated prolonged survival and induced sustained remission in a model of human AML, and has also shown effects in a number of other preclinical cancer models.

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Point Therapeutics Inc. (Nasdaq: POTP) of Boston said it has initiated a phase II trial of its lead therapeutic compound, talabostat, in combination with gemcitabine for metastatic pancreatic cancer.

The single-arm, two-stage study in up to 60 patients has a primary clinical endpoint of six-month survival, the company said. Secondary study endpoints include overall survival, progression-free survival, quality of life, and performance status.

"Overall tumor rejection rates in mice increased to 45 percent when treated with the talabostat/gemcitabine combination as opposed to a 23 percent rejection with gemcitabine alone, Don Kiepert, president and CEO of Point Therapeutics.

* * *

TransMolecular Inc. of Birmingham, Ala., said it has begun a phase II open-label, multiple-dose study of intracavitary administered 131I-TM-601 in adult patients with recurrent high-grade glioma.

The company said it would have more than 12 sites participating in the study including City of Hope National Medical Center, Florida Hospital, Northwestern University, Saint Louis University, Saint Mary's Health Care, Grand Rapids, and University of Alabama at Birmingham.

131I-TM-601 is a radiopharmaceutical containing a synthetic version of chlorotoxin, a substance derived from scorpion venom, the company said. Chlorotoxin, or TM-601, seeks out and binds to a receptor expressed on tumor cells, but not on normal cells. TM-601 acts as the guidance system that delivers a radioactive payload to its target, killing the tumor cells and minimizing collateral damage to normal cells. 131I-TM-601 has received Orphan Drug and Fast Track Development Program status from FDA, the company said.

The phase II study will be conducted in two parts, the company said. The first sequence is an open- label dose escalation, multi-dose study of four cohorts that will be treated postoperatively at escalating dose levels until the Maximum Practical Dose is reached or until

determination of the Maximum Tolerated Dose.

The second trial sequence is an open-label, randomized study in a larger group of patients that will receive either a three- or six-dose treatment cycle at determined MPD or MTD to evaluate the safety, time to disease progression and survival rates after treatment, the company said.

Deals & Collaborations:

ABG, Invitrogen Partner To Sell Technology Packages

Applied Biosystems Group (NYSE: ABI) and **Invitrogen Corp.** (Nasdaq: IVGN) of San Diego said they have formed a strategic co-marketing and re-selling alliance to deliver solutions for proteomic analyses and biomarker studies in drug discovery and disease research.

Under the alliance, the companies said they would re-sell a combined suite of labeling technologies consisting of the AB proprietary suite of protein and peptide labeling technologies—iTRAQ and ICAT reagents--and Silac, the Introgen metabolomic labeling technology. AB also said it also would provide software support for Silac on its TOF/TOF products, including 4800 MALDI TOF/TOF analyzer, and extends software support for the Silac labeling technology to other AB/MDS SCIEX protein mass spectrometry systems. The technologies and products compare relative protein expression levels between diseased and normal samples ranging from cell culture lines to tissues and serum, the companies said.

The ICAT reagents, introduced in 2001, were the first quantitative labeling strategy for protein expression analysis using LC/MS approaches (ESI and MALDI) with a focus on quantifying only proteins that contained the amino acid cysteine, the companies said. Using the iTRAQ reagents, peptides can be labeled, leading to broader protein and proteome coverage with the ability to detect post-translational modifications, and to simultaneously measure expression profiles of up to four samples, such as normal versus diseased versus drug-treated states in a single experiment. The reagents simplify the performance of proteomics experiments, such as time course studies or expression profiling studies for putative biomarkers, the companies said.

The Silac technology is a tool for quantitative analysis of differential protein expression, the companies said. The technology empowers current cell culture workflows with integration with rigorous analytical platforms. The result is a new paradigm in proteomic and cellular dysfunction analysis, the companies said. Researchers can view metabolic changes in different cell lines to compare normal versus diseased versus drug-treated.

Silac technology and ICAT reagents are both protein-labeling strategies compatible with 1D gel separation, which is the primary workflow for biologists, the companies said. Silac is used for differential protein expression analysis in cell culture samples and ICAT reagent-technology in tissue samples. iTRAQ reagents are a universal peptide based labeling approach for multiplex sample analysis.

* * *

Arrowhead Research Corp. (Nasdaq: ARWR) of Pasadena, Calif., said it has exclusively licensed intellectual property from **Stanford University** for a nanotech device that controls the behavior of adult stem cells.

Nick Melosh of the Materials Science Department at Stanford developed the technology, the company said.

Melosh is using arrays of nano-reservoirs on a chip to stimulate desired adult stem cell behavior and will conduct further research by collaborating with the Stanford Stem Cell Institute and the Lucile Packard Children's Hospital, the company said. Arrowhead said it has committed $600,000 to the project, with $110,000 funded upon signing and the remainder payable quarterly over the following two years.

"The solution we are pursuing is to build a device that can interact with the stem cell at the micro- and nanoscale," said Melosh. "For example, exposure to minute amounts of chemical at the appropriate time and place could be the key for guiding stem cells isolated from fat tissue to turn into cartilage or bone constructs."

* * *

Carna Biosciences Inc. of Kobe, Japan, and **CrystalGenomics Inc**. said it has signed a service agreement with **Rigel Pharmaceuticals Inc.** for crystallographic products and services.

The detailed, 3-D structural information for protein kinases, crystallized alone or co-crystallized with such compounds, optimizes compounds rapidly, rationally, and efficiently, the companies said.

* * *

Correlogic Systems Inc. of Bethesda, Md., said it has received an equity investment from **Quest Diagnostics Inc.** (NYSE: DGX).

Under the agreement, Quest Diagnostics retains an option to commercialize specified diagnostic tests

Correlogic is developing for certain diseases, the company said.

"The relationship with Quest Diagnostics will accelerate our delivery of pattern recognition based diagnostic tests," said Peter Levine, president and CEO of Correlogic Systems.

* * *

Bayer HealthCare, Diagnostics Division, (NYSE: BAY) of Tarrytown, N.Y., said it has granted a license to **American Diagnostica Inc**. for cancer marker assays.

Bayer said it has an exclusive worldwide license from the Danish research Foundation to market and sell PAI-1 antibodies for diagnostic use under a U.S. Patent No. 5,422,245 and 6,271,352, as well as European Patent No. 229,126). The patents relate to monoclonal antibodies and their use in assays for ePAI or PAI-1, an endothelial-type plasminogen activator inhibitor, the company said. Measurement of the substance in blood is used in cancer research, including for breast cancer.

ADI has taken a non-exclusive worldwide license under the patents to manufacture, use, sell, and offer to sell PAI-1 monoclonal antibodies and PAI-1 ELISA's for research purposes as well as for diagnostic or prognostic uses in non-tumor tissue extract assays.

This settles a patent infringement lawsuit filed jointly by Bayer and the Foundation against ADI in March 2003 in Connecticut Federal District Court.

* * *

Bayer HealthCare, a unit of the **Bayer Group** (NYSE: BAY), said it has entered into a genotyping license agreement with **DxS** and **BTG,** for the proprietary Amplification Refractory Mutation System DNA diagnostic technology for diagnostic assays, including pharmacogenetic assays.

Assays to be developed by Bayer would optimize healthcare delivery by better predicting genetic likelihood for disease onset, and by creating genetic matches for treatment therapy, the company said.

"The advent of pharmacogenetics and the increased use of molecular diagnostics as a primary tool for the diagnostician will shift healthcare to a more efficient, more cost effective system that ultimately provides enhanced care at the individual level," said John Blackwood, vice president of global new business development, Bayer HealthCare Diagnostics Division.

ARMS technology detects gene mutations and single nucleotide polymorphisms, the company said. The technology has applications in the detection of genetic variations for diseases, including cancer and heart disease. ARMS can also be used in personalized medicine tests, to predict which individuals will respond well to a medicine, and typing infectious pathogens.

* * *

Conforma Therapeutics Corp. of San Diego and **Sumitomo Pharmaceuticals Co. Ltd.** of Osaka, Japan, said they have reached a licensing agreement for Amrubicin HCl, a third-generation, totally synthetic anthracycline late-stage cancer compound.

Conforma said it has obtained exclusive rights, including sublicensing rights, to develop and market the compound in North America and Europe. Amrubicin is approved and marketed in Japan for small-cell and non-small-cell lung cancer under the brand name Calsed, the companies said. Sumitomo would manufacture the product for worldwide distribution.

"Pre-clinical and clinical data suggest that Amrubicin is not only more active than traditional anthracyclines but also appears to be free of the cumulative cardiotoxicity which has limited the utility of this class of drugs," said Robert De Jager, vice president, clinical research and development and chief medical officer of Conforma.

Marketing approval was given in Japan in December 2002, the companies said. Phase II trials in the U.S. and Europe will begin in early 2006.

* * *

Exact Sciences Corp. (Nasdaq: EXAS) of Marlborough, Mass., and **OncoMethylome Sciences** of Durham, N.C., said they have entered into a research collaboration to evaluate gene methylation markers for use with the Exact next-generation, non-invasive colon cancer screening technology.

The markers were identified at Johns Hopkins University and are exclusively licensed to OncoMethylome Sciences, the company said.

"By working with the leader in the field of non-invasive DNA-based colorectal cancer detection we will further solidify the vast potential of our Methylation-Specific PCR technology and our patented genes in the field of cancer diagnosis and personalized medicine," said Herman Spolders, CEO of OncoMethylome Sciences.

* * *

Exelixis Inc. (Nasdaq: EXEL) of South San Francisco and **Helsinn Healthcare S.A.** of Lugano, Switzerland, said they have reached an agreement to develop XL119 (becatecarin) for biliary tract cancers.

Under the agreement, Helsinn will pay Exelixis an upfront payment of $4 million and additional milestones up to $21 million, the companies said. In addition, Helsinn will assume the cost of the phase III program. In return, Exelixis has granted to Helsinn a world-wide,

royalty-bearing license to XL119. Exelixis has retained rights to reacquire commercial rights to XL119 for North America, and will receive milestones and royalties on sales in the rest of the world.

"The agreement will free up substantial financial and product development resources, allowing Exelixis to focus on the phase I and II trials for our internally developed pipeline," said George Scangos, president and CEO of Exelixis. "At the same time, we have structured the deal with rights to reacquire the commercial rights to XL119 for North America, which is our primary market."

The agent is in a multi-national phase III trial at 50 centers in North America and Europe, the companies said. The primary endpoint of the 600-patient trial is increased survival for bile duct tumors treated with XL119 compared with the chemotherapy agents 5-fluorouracil and leucovorin. XL119 was granted orphan drug designation in the USA in March 2004, the companies said.

* * *

GeneGo Inc. of St. Joseph, Mich., said NCI has licensed MetaCore 2.5, the GeneGo platform for mining of high-throughput experimental data.

NCI researchers will be able access the platform in house through their web browser and will be able to analyze multiple types of small to genome scale experimental datasets, the company said.

The latest version of MetaCore 2.5, released in May 2005, is based on the largest curated database of mammalian biology and physical protein interactions, the company said. Features include multiple network building algorithms and filters; maps with established metabolic and signaling pathways; advanced network comparison option; statistical cross-referencing and scoring between networks, pathways and functional processes; custom pathway editor.

* * *

Ligand Pharmaceuticals Inc. (Nasdaq: LGNDE) of San Diego said it has earned a $2 million milestone payment from **GlaxoSmithKline** (NYSE: GSK) with the Glaxo filing of IND for SB-559448, a small-molecule drug that mimics the activity of thrombopoietin, a protein factor that promotes growth and production of blood platelets.

Thrombocytopenia, decreased platelet count, is a side effect of many chemotherapies and can lead to uncontrolled bleeding, thus representing a significant problem in the treatment, the company said. Similarly, thrombocytopenia is seen myeloablative therapies or for leukemias or metastatic tumors.

SB-497115, a non-peptide small molecule TPO receptor agonist with demonstrated activity in human bone marrow in vitro assays and pharmacological activity in humans, is being developed for thrombocytopenia associated with chemotherapy or disease states such as immune thrombocytopenic purpura and chronic liver disease, the company said.

* * *

Miraculins Inc. of Winnipeg, Manitoba, said it has acquired intellectual property assets of **Europroteome AG**, a former developer of diagnostic, prognostic, and patient specific therapy products for cancers.

The acquired property portfolio includes 14 patents and discoveries, and utilizes the human sample collection of Europroteome, which contains samples from 4,000 patients, the company said.

Europroteome AG said it is one of the first companies in the world to link molecular data and clinical information on a patient-by-patient basis by utilizing its clinical cancer network of clinicians, academic institutions and oncology scientists, the company said. Owing to fundraising problems, Europroteome filed for creditor protection under the German Insolvency Act and subsequently and entered receivership in the latter part of 2004.

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The Molecular Profiling Institute Inc. said it has acquired the assets of **NanoBiomics Inc**. Both companies are based in Phoeniz, Ariz.

NanoBiomics is developing genomic-based diagnostics using nanoscale-processing technologies created at the Applied Nanobioscience Center at Arizona State University.

NanoBiomics was formed by the Translational Genomics Research Institute and Arizona Technology Enterprises with the intention to commercialize technology from both organizations. Molecular Profiling, a collaboration between TGen and the International Genomics Consortium, is a specialty reference laboratory and a leader in using genetic signatures to help tailor medical therapy. Molecular Profiling is the first for-profit spin-off venture for TGen and IGC.

"The acquisition provides Molecular Profiling with a platform for commercializing novel, genomic-based diagnostic products in the future," said Richard Love, acting president of NanoBiomics and managing director of TGen Accelerators. "Molecular Profiling is currently driving physician adoption of such tests in the reference lab setting. As these tests are accepted into the practice of medicine, NanoBiomics' technologies

will help enable lower cost diagnostic products to be produced and commercialized more broadly."

Molecular Profiling will work with Frederic Zenhausern, director of the Applied Nanobioscience Center at ASU's Biodesign Institute.

"Dr. Zenhausern is a pioneer in using nanoscale processing technologies to perform complex biological processes on cartridges the size of credit cards," said Robert Penny, CEO of Molecular Profiling. "These technologies will ultimately drive down the cost of genomic-based diagnostic testing and this transactions will provide a commercial focus for the collaboration to enhance the collaboration between TGen, IGC, and ASU at Molecular Profiling."

The acquisition brings together the diagnostic platform developed by ASU, the diverse and extensive database of DNA signatures and scientific leadership from TGen, and the reference laboratory expertise and market access offered by Molecular Profiling, the entities said.

"The complementary technologies that Molecular Profiling, Tgen, and NanoBiomics bring to bear create a stronger molecular diagnostics products and services company with a clear commercialization path," said Peter Slate, the CEO of AzTE. "This is a case where the sum is worth substantially more than the individual parts."

The terms of the acquisition were not disclosed.

* * *

SD Pharmaceuticals Inc. of Carlsbad, Calif., said it has begun an out-licensing effort on its proprietary nano-emulsion formulations for intravenous drugs for cancer and infectious disease.

The formulations are designed to improve the safety profile and remove black box warnings on four marketed important drugs, which suffer from formulation related adverse effects, the company said.

"Our business strategy is to engage in partnerships with other pharmaceutical companies that have the ability to market our products and complete the necessary regulatory filings to gain approval," said Paul Marangos, chairman and CEO of SD Pharmaceuticals.

* * *

Siemens Medical Solutions of Siemens AG (NYSE: SI) of Malvern, Pa., said **Mayo Clinic** of Rochester, Minn., has installed its Somatom Sensation Open computed tomography system for advanced imaging capabilities for its bariatric surgery program.

The system, which has 40-slice technology, is an optional high-capacity patient table, developed as part of the Clinical Innovation Center partnership between Mayo Clinic and Siemens, the company said. The SSO will be used for image-guided interventional procedures, and cancer and routine diagnostic imaging.

With an 82-centimeter large gantry bore and 82-centimeter extended field of view, the SSO allows visualization of the entire anatomy, especially for patients weighing up to 615 pounds, compared to 440 pounds for conventional patient tables, the company said.

"The system has the clinical and technical attributes we were seeking especially for bariatric care and image guided interventions," said Cynthia McCollough, associate professor of radiological physics, Mayo Clinic College of Medicine.

In the agreement, there would be a delivery of eight high-end systems, including seven Somatom Sensation 64 scanners, the company said.

The Somatom Sensation Open is a large bore 40-slice system, with a 0.5 second gantry rotation speed and the Siemens proprietary z-Sharp Technology, the company said. An electron beam is deflected, creating two alternating and overlapping X-ray projections reaching each detector element. This doubles the scan information without a corresponding increase in dose, resulting in enhanced spatial resolution and image quality.

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StemCo Biomedical Inc. of Durham, N.C., said it has signed a worldwide distribution agreement whereby **StemCell Technologies** of Vancouver, British Columbia, will distribute the StemCo Aldefluor product.

The Aldefuor kit identifies stem and progenitor cells for research using the StemCo proprietary ALDH-based technology, the company said. Aldehyde dehydrogenase is an intracellular enzyme found in stem and progenitor cells.

The product is manufactured under GMP and has been marketed since 2003 as a Research Use Only reagent, the company said.

* * *

Theragenics Corp. (NYSE: TGX) of Buford, Ga., said the parties have settled the arbitration case filed by **Oncura** in 2003 by mutual consent.

As part of the settlement, each party has dropped its claims against the other and the parties agreed to advance the termination of their distribution agreements for TheraSeed, the palladium-103 cancer treatment device, the company said.

The TheraSeed device will continue to be marketed and sold through Theragenics as well as through its remaining distributor, the company said.