THE CANCER LETTER

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Money Would Speed Progress, NCI Says, But Backs Off Meeting 2015 Goal by 2010

By Kirsten Boyd Goldberg

In a plan submitted to Senate appropriators, NCI Director Andrew von Eschenbach said that additional money would make it possible for the Institute to beat its previously stated goal to "eliminate suffering and death due to cancer" by 2015.

To "accelerate progress," NCI would need another $4.2 billion over five years, von Eschenbach wrote, responding to a question from Sen. Arlen Specter (R-Pa.), chairman of the Senate Labor-HHS Appropriations Subcommittee.

The response backs away from the projection von Eschenbach made at a Senate hearing earlier this year, when he said his 2015 goal could be met by the year 2010. "While the elimination of suffering and death due to cancer may not be fully achievable by 2010, there would be significant progress toward narrowing the gap between 2015 and 2010," the document said.

Von Eschenbach's four-page respose to Specter went through clearance by NIH and HHS and was released last week.

The NCI director was less equivocal in his Congressional testimony. "We would be able to accelerate the pace of progress and close that gap, in

(Continued to page 2)

Obituary:

Sir Richard Doll, Epidemiologist Linked Smoking To Lung Cancer

Sir Richard Doll, the epidemiologist whose research established the causative association between smoking with lung cancer, died July 24 at the John Radcliffe Hospital in Oxford after a short illness. He was 92 and was the former Regius Professor of Medicine at Oxford University.

In 1950, Sir Richard and Austin Bradford Hill, of the Medical Research Council, published their findings in the British Medical Journal on a survey of lung cancer patients in London hospitals. The study found that smoking was the only factor overwhelmingly implicated in lung cancer.

"The risk of developing the disease increases in proportion to the amount smoked," the report concluded. "It may be 50 times as great among those who smoke 25 or more cigarettes a day as among non-smokers."

In 1951, Sir Richard and Hill began a study that continued for 50 years, asking more than 34,000 doctors in Britain about their smoking habits and then tracking their health. The early results confirmed that smokers were much more likely to die of lung cancer than were non-smokers.

(Continued to page 8)

The NCI 2010 Plan:
Exchanges With Specter Show Progression Of 2010 Plan, Von Eschenbach's Use Of Survival Rate As Measure of Progress
. . . Page 2

Additional Funding Would Be Used For Advanced Tech, Centers, Clinical Trials
. . . Page 4

Commentary:
Use Cancer Mortality, Not 5-Year Survival, To Measure Progress
. . . Page 6

Funding Opportunities:
Leukemia & Lymphoma Society Offers Awards
. . . Page 7

NCI Director Says Progress Determined By 5-Year Survival

(Continued from page 1)

my opinion," he said at a Senate appropriations hearing May 11.

At that time, von Eschenbach said NCI would need $3 billion over five years to meet what would become the 2010 goal. In the written document, the price went up by $1.2 billion. NCI's current budget is $4.8 billion.

The new money would be used for a National Advanced Technology initiative for cancer, including projects in molecular oncology, nanotechnology, and bioinformatics, the document states. Also, NCI would improve its clinical trials infrastructure and expand its Cancer Centers Program from 60 centers to 75.

The plan doesn't specify how NCI would determine when "suffering and death" has been eliminated. However, the document states that improvements in cancer survival will result in "lives saved."

It would be wrong to assume that increases in cancer survival translate into declines in cancer mortality, experts say. The five-year survival rate is a measurement of how many people diagnosed with cancer are alive five years later. Greater cancer awareness and screening have lengthened the time between diagnosis and death, but there is little correlation between cancer survival rates and cancer mortality rates.

"What Would It Take To Move The Goal Back?"

The exchanges between Specter and von Eschenbach at two hearings last spring show the NCI director's movement toward the 2010 goal and, for the first time, clarify that he is relying on five-year survival as the measure of progress.

At an NIH budget hearing April 6, Specter, who had lost his hair due to chemotherapy treatment for Hodgkin's lymphoma, asked von Eschenbach whether NCI had sufficient funding to reach its 2015 goal.

VON ESCHENBACH: "The funding that we have, we are applying as effectively and efficiently as possible to achieve that trajectory. Obviously, with increased resources, we have increasing opportunities to even further accelerate the pace of progress."

SPECTER: "If your funding were increased, could you reduce that date to 2010?"

VON ESCHENBACH: "We certainly could accelerate the pace of progress, and how soon we could bring that about, I could not absolutely predict."

SPECTER: "I would like you to give that some thought, and provide the subcommittee with a projection as to what kind of funding you would require to reduce the figure to 2010. A lot of people are going to have a lot of suffering in those other five years."

At a May 11 hearing on gynecological cancers, Specter followed up. "President Nixon declared war on cancer in 1971, and we could have won this war long ago," he said. "This has been on my mind long before I had a personal involvement. My new hair styling is not voluntary. It's a result of a temporary bout with Hodgkin's."

VON ESCHENBACH: "The National Cancer Institute has set a goal that by the year 2015, we will eliminate not cancer, but we will eliminate the suffering and death due to cancer."

SPECTER: "When you cite the year 2015, what will occur by then, at least according to your current projections?"

VON ESCHENBACH: "As we sit here today, Senator, two out of three patients who hear the words, 'You have cancer,' can look forward to being a cancer survivor. We intend to close that gap. We will close that gap across the continuum of discovering more about cancers' mechanisms."

SPECTER: "What is going to happen by 2015 as you project it?"

VON ESCHENBACH: "No one who hears the words, 'You have cancer,' will suffer or die from the disease. We will prevent and eliminate the outcome."

SPECTER: "So you will move from two out of three survivors to all three?"

VON ESCHENBACH: "Yes, sir."

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SPECTER: "What is the budget now of NCI?"

VON ESCHENBACH: "$4.8 billion."

SPECTER: "When you appeared here last, just a few weeks ago, I asked you what it would take to move that date up to 2010."

VON ESCHENBACH: "Yes, sir."

SPECTER: "You have had several weeks to prepare your answer."

VON ESCHENBACH: "Yes, sir."

SPECTER: "What is your answer?"

VON ESCHENBACH: "The answer has been submitted to you, sir, for the record, and is going through process through NIH and the Department, as it is being submitted officially to the Congress and to you specifically."

SPECTER: "OK, so tell me what the answer is."

VON ESCHENBACH: "There are three parts to the answer. One is to embrace the National Advanced Technology Initiative for cancer. The second was to expand our Cancer Centers Program network by the addition of 15 more cancer centers. And the third part of the equation was the expansion and integration of our clinical research infrastructure."

SPECTER: "What will it cost?"

VON ESCHENBACH: "We have a proposed budget that would support those initiatives that would amount to approximately $600 million a year."

SPECTER: "Six hundred million dollars a year?"

VON ESCHENBACH: "Yes, sir."

SPECTER: "Extra?"

VON ESCHENBACH: "Yes, sir."

SPECTER: "And you can move the date from 2015 to 2010?"

VON ESCHENBACH: "We would be able to accelerate the pace of progress and close that gap, in my opinion."

SPECTER: "OK. Well, that's the kind of specificity we like to have."

Survival Doesn't Mean "Lives Saved"

"The idea that 'no one who hears the words, 'You have cancer,' will suffer or die from the disease' is outrageous," said Steven Woloshin, Lisa Schwartz, and H. Gilbert Welch, of the VA Outcomes Group, VA Medical Center, in White River Junction, Vt., in an email to The Cancer Letter. "It grossly exaggerates what is realistically achievable. Furthermore, it undermines the credibility of science by setting an unachievable goal."

The experts go on to raise questions about the connection between cancer survival and mortality. According to NCI's 2010 plan, increases in cancer survival will result in improved mortality. "Incremental improvements in survival will continue toward our 2015 goal, but we can accelerate these gains," the document states. "Even improving the overall survival rate to 90 percent by 2010 could mean an additional 850,000 lives saved."

This statement is misleading, because it wrongly equates improved survival for cancer patients with the saving of lives, the three physician-researchers said. "This is a common problem, as progress in the war against cancer is typically reported in terms of improvements in five-year survival," they said.

Improvements in five-year survival are strongly related to changing patterns of diagnosis, said the researchers, who also are affiliated with Dartmouth Medical School. Increasing cancer awareness and screening may lengthen the time between diagnosis and death and may diagnose more people with early cancer, but may not affect mortality rates. (See related story on page 6).

"In a recent study of trends since 1950, we found no relationship between changes in five-year survival and changes in mortality for the most common tumors in the U.S. [JAMA, 2000]," Woloshin, Schwartz, and Welch said. "In fact, the tumor with the largest drop in mortality, stomach cancer, had only a trivial change in five-year survival (from 12% to 19%). And the two tumors with the most dramatic increases in five-year survival, prostate cancer (from 40% to 94%) and melonoma (from 49% to 88%), mortality rates were either stable or rising."

In their JAMA paper, the researchers concluded: "To measure true progress in the 'war against cancer,' physicians and policymakers should focus on mortality."

Field "Energized" By Goal?

Neither NIH nor Congress has acknowledged NCI's 2015 goal until recently, three years after von Eschenbach announced it. NIH Director Elias Zerhouni discussed it for the first time publicly in an interview published in the June 3 issue of Science. He distanced himself from the goal, describing it as NCI's "way to energize their field."

In the past month, House and Senate appropriations committees have endorsed the goal for the first time in their reports attached to budget bills (The Cancer Letter, July 22 and July 1.) The Senate committee requested that NCI prepare a formal report on "specific steps that

must be taken to achieve this goal by 2010."

The American Association for Cancer Research issued a position statement in support of the goal. Many groups, while supporting NCI's bypass budget requests, haven't made statements about 2015.

Nobel laureate Harold Varmus, president of Memorial Sloan-Kettering Cancer Center and former NIH director, has called the 2015 goal unrealistic. "Notwithstanding the enthusiasm of ... Dr. von Eschenbach, we have a long way to go before we beat cancer," Varmus said at the annual meeting of the American Society of Clinical Oncology last May. "We are not going to do so by 2015."

Addressing the 2015 goal more technically, the National Cancer Policy Board, in a 2003 report, said stepped-up cancer prevention, primarily through behavioral changes such as smoking cessation, could achieve a 19-percent decline in cancer incidence and 29-percent decline in cancer mortality by 2015. These efforts would prevent 100,000 cancer cases and 60,000 deaths annually, the board said (The Cancer Letter, March 28, 2003, Vol. 29 No. 13).

The 2010 Plan

The text of NCI's plan appears below and is available at http://www.cancer.gov/NCICancerBulletin/NCI_Cancer_Bulletin_071905.

What would it take to accelerate the achievement of the NCI's 2015 goal to eliminate suffering and death due to cancer from 2015 to 2010?

You have requested information on the amount of money necessary for the National Cancer Institute to achieve its 2015 goal by 2010. It should be noted, though, that these funding estimates for additional resources were developed without taking into consideration overall fiscal constraints and other competing priorities of the National Institutes of Health, the Department of Health and Human Services, or the rest of the Federal government over this 5-year time period. The current annual NCI budget is nearly $5 billion and the resources discussed below would be in addition to this base.

NCI has established an ambitious goal of eliminating the suffering and death due to cancer by 2015 by sustaining and integrating progress in the discovery, development, and delivery of more effective interventions based on molecular mechanisms of cancer. We estimate that expenditure of an additional $4.2 billion above the NCI base of nearly $5 billion over the next 5 years could accelerate progress. While the elimination of suffering and death due to cancer may not be fully achievable by 2010, there would be significant progress toward narrowing the gap between 2015 and 2010.

This $4.2 billion estimate reflects an additional upfront allocation of $2.5 billion to be expended over 5 years for a National Advanced Technology Initiative for cancer (NATIc) to accelerate the emerging disciplines of molecular oncology, nanotechnology, and bioinformatics for use in creating a pipeline of new personalized cancer diagnostics and therapeutics. This would also reflect an annual increase of $171 million over current base NCI levels for 5 years to deploy a modern integrated cancer clinical trials infrastructure and an annual increase of $164 million for 5 years to expand and integrate the NCI-designated Cancer Centers program from 60 existing centers to 75. In addition to resources, additional legislative authorities related to exemptions from specific parts of current procurement, grant review and processing, and licensing and patenting rules would also help speed progress toward an accelerated cancer goal.

Three decades ago there were 3 million U.S. cancer survivors; today that number has increased to over 10 million. Today, each minute of every hour of every day, 1 American dies from cancer: 570,280 lives will be lost this year due to this disease. Despite this fact, there has been remarkable progress in understanding the cancer process and applying that knowledge. Today, 65 percent of patients diagnosed with cancer can expect to survive. If we had the ability to apply what we know today to every cancer patient, we could have an immediate impact on survival, largely through the NCI Cancer Centers. Incremental improvements in survival will continue toward our 2015 goal, but we can accelerate these gains. Even improving the overall survival rate to 90 percent by 2010 could mean an additional 850,000 lives saved. The impact of this strategy could produce annual changes in the first 2 years of around 2 to 3 percent with larger increases occurring in 2008-10.

For most cancer patients, survival is greatly influenced by early detection. The rapid deployment of advanced imaging, nanotechnology-supported early detection platforms, and targeted therapies will change the face of diseases such as ovarian, lung, colon, and breast cancers, where survival is low because we can not currently detect them before they spread. Ovarian cancer, which is very difficult to detect and diagnose in its early stages, has over 25,000 new cases diagnosed annually and over 14,000 deaths; the mortality rate is nearly 85 percent. Imaging and detection techniques presently under development and broadly applied could reverse that mortality rate to be an 85 percent survival

rate. Lung cancer, with approximately 170,000 expected deaths this year, would see a significant reduction in the number of deaths if the application of new technologies combined with other interventions could be universally applied in an accelerated manner.

The challenge to achieving the goal of eliminating the suffering and death due to cancer by 2010 is daunting, but with the authorities and appropriations commensurate with the task, the pace of progress could be accelerated, and the gap between 2015 and 2010 narrowed. The following reflects a brief overview of how such funds, if available, could be applied.

•Rapid Deployment of a National Advanced Technology Initiative for Cancer: $2.5 billion one-time appropriation with commensurate authorities.

•Deployment of a Modern Integrated Clinical Trials Infrastructure: $171 million addition to the NCI base budget.

•Expansion and Integration of the Cancer Centers Program: $164 million addition to the NCI base budget.

•Mechanisms and Flexibilities: streamlined procurement and review processes to acquire materials and services; coordination of licensing and patenting activities.

A National Advanced Technology Initiative for cancer (NATIc) could provide a linkage between the National Cancer Program and research and development (R&D) initiatives being developed in selected national laboratories and advanced technology facilities located in more than 40 states and regions. Connected in real time through a common bioinformatics grid, NATIc could serve as a "network of networks" of science, technology, and treatment to accelerate the emerging discipline of molecular oncology to create a pipeline of new personalized cancer diagnostics and therapeutics from bench concept to bedside and community delivery. In the next few years, such an initiative could:

•Accelerate the implementation of a nationwide high-end information technology grid for bioinformatics that could be uniquely adapted for real-time data sharing. NCI's pilot version, the Cancer Biomedical Informatics Grid, called caBIG, is currently being implemented among 50 cancer centers, the Food and Drug Administration, and other organizations.

•Develop a comprehensive biomarker discovery and validation program.

•Foster the application of emerging technologies, such as nanotechnology, and integrate molecular agents with advanced imaging devices.

•Accelerate a nationwide "real-time" medical information electronic system for research and medical data sharing using technologies and devices currently employed by the banking industry and large-scale commercial enterprises.

•Enhance the discovery and validation of new targets of genes and proteins critical to cancer development.

NCI could deploy a more modern and integrated infrastructure for cancer clinical trials. This clinical research infrastructure could:

•Strengthen collaborations with industry, FDA, the Centers for Medicare and Medicaid Services, and other public, private, academic, and patient advocacy organizations to oversee the conduct of cancer clinical trials.

•Develop new infrastructure and procedures to standardize, coordinate, and track clinical trials development and accrual across all NCI-supported clinical trials.

•Increase utilization of imaging tools in screening and therapy trials, evaluate new imaging probes and methodologies, enable access to the imaging data from trials in an electronic format, and facilitate evaluation of image-guided interventions.

•Expand access and improve the timeliness for completion of the highest priority clinical studies.

•Foster the development of a cadre of established clinical investigators who could work between bench and bedside.

•Pilot new approaches and develop prototypes for clinical trials networks that could improve the efficiency, coordination, and integration of our national efforts.

•Develop a common clinical trials informatics platform that could be made available to the full range of investigators working within the cancer clinical trials system.

NCI could accelerate the expansion and integration of the NCI-designated Cancer Centers program, including the addition of 15 new cancer centers, increasing the number of centers from the current 60 to 75. The Cancer Centers program could:

•Implement progressive bioinformatics and communication systems to achieve horizontal integration.

•Fund additive programs in collaborative, multidisciplinary research and require integration and sharing of results.

•Broaden the geographic impact of the centers, networks, and consortia and vertically integrate them with community and regional health care delivery systems.

•Improve the access of minority and underserved populations to state-of-the-art research and resources.

•Create and strengthen partnerships with government agencies and community organizations.

•Broadly provide expertise and other resources to caregivers, patients and families, and appropriate health agencies.

In addition to appropriations, flexible legislative authorities related to exemptions from specific parts of current procurement, grant review and processing, and licensing and patenting rules could also help accelerate progress. A streamlined procurement process could facilitate the acquisition of materials and services to support the R&D activities. Technology development could also be enhanced by sufficient flexibility and integration to enable interactions among a wide array of laboratories and other entities. Expedited review procedures and work flow processing could help to award funds in sequence as needed. This might include direct solicitation from known laboratories or other sources of technology, and the capability to terminate funding instruments at the convenience of the government with limited appeal processes so that funds could be redirected from low-performing consortia to more productive venues.

Coordination of the licensing and patenting activities among grantees, contractors, and the intramural program could also be useful for many of the multicomponent technology platforms that could be created through this effort. An accelerated process for Determination of Exceptional Circumstances and deviations from appropriate Federal Acquisition Regulation clauses, when deemed valuable to the broad research enterprise, could be utilized.

Survival Is The Wrong Statistic To Track "War On Cancer"

The Cancer Letter asked physician researchers Steven Woloshin, Lisa Schwartz, and H. Gilbert Welch, of the VA Outcomes Group, VA Medical Center, White River Junction, Vt., to comment on the use of survival as a measurement of progress in the NCI's 2010 plan. Their full remarks appear here.

"Even improving overall survival rate to 90 percent by 2010 could mean an additional 850,000 lives saved."

The author of the statement wrongly equates improved survival rates for cancer patients with the saving of lives. This is a common problem as progress in the war against cancer is typically reported in terms of improvements in "five-year survival."

To understand why five-year survival may not mean what you think, you have to understand the statistic. Five-year survival is the proportion of individuals with cancer who are alive five years after receiving the diagnosis. For example, the statement, "The 94% five-year survival for prostate cancer," means that if 1,000 men were diagnosed with prostate cancer in 2000, 940 would be alive in 2005.

The numerator—number alive—is unambiguous. People are either alive or dead. The denominator—all patients with disease—is not so straightforward: it depends on when patients are diagnosed and how many are diagnosed with early cancer. "When" patients are diagnosed varies over time. In the past, cancer was detected when people developed symptoms (e.g., weight loss, coughing blood, etc.). At that point, the cancers had generally grown to be large, or spread throughout the body. With improved diagnostic technology, it is increasingly possible to diagnose cancer early, when it is small and localized, well before symptoms develop. In fact, that is the whole point of screening tests like mammograms, colonoscopies, and pap tests.

The problem is that anything which lets us diagnose cancer early plays havoc with five-year survival statistics. Why? Because by definition, five-year survival is measured from time of diagnosis. So anything that advances the time of diagnosis (e.g., a screening test) must improve five-year survival—even if no patient lives a second longer.

Because this idea is counter-intuitive, it is sometimes helpful to consider some simple thought experiments. Imagine a group of 1,000 men diagnosed with lung cancer (because of weight loss, cough, etc.) at age 77; despite the best care they all die by age 80. For these men the 5-year survival is 0% (0 men survive 5 years from the time of diagnosis). Now imagine there is a test which can find the lung cancer when the men are all 74 years old and feeling well. Even if nothing else changes, even if every man still dies at age 80, even if no man lives one second longer, five-year survival increases dramatically. In fact, it is 100%. But not a single life was saved.

There is another way to improve five-year survival without saving lives: early detection, which results in more patients being found with milder forms of cancer. People generally think of cancer as a relentlessly progressive disease. But not all cancers are the same. Some grow fast (people with aggressive cancers get sick quickly and have the worst prognosis) but some grow very slowly. Some do not grow at all. These

non-progressive cancers never cause symptoms and the individual ends up dying from something else entirely. Evidence for such non-progressive cancers comes from autopsy studies which show that it is often possible to find indolent cancers in people who have died from other causes. Non-progressive cancer also distorts five-year survival statistics.

For example, imagine again 1,000 men diagnosed with cancer because of symptoms. Despite the best care, imagine that 600 die within five years; that is, their five-year survival is 400/1000 or 40%. Now imagine that an additional 1,000 men are diagnosed with non-progressive cancers. Now, 5 years later there will be 1,000+400 alive divided by 1,000+1,000 cancer patients, for a five-year survival of 70%. But again, not one life was saved.

It is not necessary to use a thought experiment to show that changes in survival over time do not imply changes in mortality. In a recent study of trends since 1950, we found no relationship between changes in five-year survival and changes in mortality for the most common tumors in the U.S. [JAMA, 2000]. In fact, the cancer with the largest drop in mortality, stomach cancer, had only a trivial change in five-year survival (from 12% to 19%). And the two cancers with the most dramatic increases in five-year survival, prostate cancer (from 40% to 94%) and melonoma (from 49% to 88%), mortality rates were either stable or rising.

"Three decades ago there were 3 million U.S. cancer survivors; today that number has increased to over 10 million."

The author of this statement assumes that more cancer diagnoses is good news. And it may be. But it is also possible that some of the cancers detected are of the non-progressive type (or an epidemic of cancer). Then the news is not so good. People with non-progressive cancer can only be harmed by diagnosis and (by definition) unnecessary treatment. Increasing numbers of survivors is only good news if fewer people are dying from cancer.

We are not saying that there has been no progress made against cancer. Nor are we saying that five-year survival rates are useless; they are useful if the time of diagnosis is the same for the groups being compared as in a randomized trial.

We are saying that improved survival is not the same as saving lives. It is the wrong statistic to use to track progress against cancer.

The Cancer Letter welcomes short commentaries and Letters to the Editor.

Funding Opportunities:

Leukemia & Lymphoma Society Offers Awards

Specialized Center of Research Grant Program for 2006. Preliminary Application (submitted via Web site): Nov. 1. Full application from Selected Investigators Due Date: March 15.

Leukemia & Lymphoma Society has begun a program to bring together research teams and promote interdisciplinary research on leukemia, Hodgkin's and non-Hodgkin's lymphoma, and myeloma. The center must be composed of at least three relevant scientific projects capable of interacting. The research may be fundamental or applied, or an integrated combination. Basic research tied to a related translational research project is encouraged, but not mandatory. The center grant will also support scientific core laboratories required by the component research programs.

Application may be submitted by an M.D., Ph.D., or equivalent degree, in a domestic or foreign non-profit organization.

The annual total cost of the center, direct and indirect, cannot exceed $1.25 million. The aggregate costs over five years cannot exceed $6.25 million. The direct costs, if justified by the aggregate budget, may be up to $1.042 million per year. The indirect or institutional costs cannot exceed 20 percent of the direct costs per year.

Leukemia & Lymphoma Society Scholar/Fellows. Preliminary Application Deadline (submit via Web site): Sept. 15. Full Application Deadline: Oct. 1.

Scholar Awards: Five-year stipend of $105,000 plus $5,000 annual institutional overhead for leukemia, lymphoma, and myeloma research. Investigators are expected to hold independent faculty-level or equivalent positions and have concomitant support from another source or agency.

Special Fellow: Three-year stipend of $56,000 plus $4,000 annual institutional overhead for qualified investigators who have completed a minimum of two years of postdoctoral research training at the time of review (Jan. 31) and are continuing research under the direction of a research sponsor.

Special Fellow in Clinical Research: Three-year stipend of $56,000 plus $4,000 annual institutional overhead for qualified investigators who have completed a minimum of two years of clinical hematology, oncology, hematology/oncology or hematopathology training or postdoctoral research training in a clinical discipline, and require research training to conduct future independent clinical research

Fellow: Three-year stipend of $47,000 plus $3,000 annual institutional overhead for investigators with less than two years of postdoctoral research training (as of Jan.31).

Inquiries: director of research administration, Leukemia & Lymphoma Society, 1311 Mamaroneck Ave., White Plains, N.Y. 10605, phone 914-821-8859; e-mail researchprograms@LLS.org. Guidelines are available from www.LLS.org.

Sir Richard Doll, 92

(Continued from page 1)

The research moved to Oxford University when Sir Richard was appointed Regius Professor of Medicine, the university's most senior medical post, in 1969. The 20, 40, and 50-year results, published in collaboration with Sir Richard Peto, showed that half of all persistent smokers were eventually killed by their habit, but that stopping smoking cut the risks.

The research also showed that smoking could cause other types of cancer, as well as heart disease, respiratory disease, and peptic ulcer.

"Richard Doll's work has prevented millions of premature deaths in the 20th century, and will prevent tens of millions of premature deaths in the present century," Peto said. "He was unique in medical history."

In 1979, he became the first warden of Green College and director of the Cancer Epidemiology Unit. He retired from administrative work in 1983, but continued his research in the Clinical Trial Service Unit, co-directed by Peto and Rory Collins. The 50-year follow-up of the British Doctors' Study was published when Sir Richard was 91: www.mrc.ac.uk/public-22_June_2004.

"Sir Richard's enormous contribution to medicine globally, and within Oxford, cannot be overstated," said John Hood, vice-chancellor of the university. "His pioneering epidemiological work on the link between smoking and cancer, cardiovascular disease and many other disorders, has led to the dramatic reduction in smoking rates in Britain over the past 50 years, especially among men. This research has saved many millions of lives."

The university will open the Richard Doll Building later this year, bringing together the Clinical Trial Service Unit and the Cancer Epidemiology Unit.

Sir Richard graduated in 1937 from St. Thomas's Hospital Medical School in London. During World War II, he served in the Royal Army Medical Corps. He moved to the Central Middlesex County Hospital in 1946, working in the new field of epidemiology. In 1948, he joined the Statistical Research Unit of the Medical Research Council, becoming its deputy director in 1959 and director from 1961 to 1969.

He was knighted in 1971 and became a Companion of Honour in 1996.

Sir Richard married Joan Mary Faulkner, in 1949. She died in 2001. He is survived by their son and daughter.

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:

OTN To Sponsor Programs On Medicare By Community Oncology Alliance

Oncology Therapeutics Network of South San Francisco said it would provide sponsorship for Community Oncology Alliance to conduct general educational programs, communications, and community meetings in its campaign to soften the impact of Medicare reimbursement changes for office-based oncologists.

The sponsorship of COA would continue through 2006.

Founded in 2003, COA represents community oncology practices

(Continued to page 2)

Product Approvals & Applications:

Mentor Receives Approvable Notification From FDA For Silicone Breast Implants

Mentor Corp. (NYSE:MNT) said it has received an "approvable letter" from the U.S. Food and Drug Administration for the company's MemoryGel silicone gel-filled breast implants.

The approvable letter stipulates a number of conditions which Mentor must satisfy in order to receive FDA approval to market and sell silicone gel-filled breast implants in the United States.

"We are very encouraged by this communication from the FDA, and view this letter as a positive sign for women and their surgeons that another option will soon be available," said Joshua Levine, president and CEO of Mentor. "We thank the FDA and its advisory panel for the rigorous and objective review of our data and related science."

"For more than a decade, choices for women seeking breast augmentation and reconstruction have been limited," said Levine. "If ultimately approved by the FDA, Mentor's Memory Gel breast implants will be a significant additional option for these women. Mentor is committed to making these important products available to women and will continue working with the FDA to address the approvable conditions."

Previously, on April 13, the FDA's General Plastic Surgery Devices Advisory Panel recommended Mentor's MemoryGel breast implants for approval with conditions by a vote of 7 to 2. The vote was based primarily upon its review of Mentor's pre-market approval application filed in December 2003 and on the company's PMA amendment filed in August 2004.

(Continued to page 3)

Clinical Trials:
Agensys Submits IND For Phase I Trial Of Monoclonal Antibody
. . . Page 4

Deals & Collaborations:
Merck To Buy Rights To UFT From Taiho For Colon Cancer
. . . Page 6

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OTN Grant To Help Alliance Develop Educational Programs

(Continued from page 1)

across the U.S. Many Washington observers view it as a challenger to the leading role the American Society of Clinical Oncology has played on the reimbursement issues.

"Recent initiatives have led to a change in reimbursement for community cancer care that could place patient access to care at risk," said Leonard Kalman, medical oncologist in Florida and president of COA. "OTN's grant allows us to continue our educational efforts about how to protect access to high-quality, affordable cancer care, which is a hallmark of cancer treatment delivered in the community setting."

OTN said it is partnering with COA to inform the community about Medicare reimbursement of cancer drugs and initiatives to change reimbursement of cancer therapies, such as the Competitive Acquisition Program.

"By supporting COA, we are helping fulfill our mission of providing community-based oncologists with the information, services, technology and support they need to adapt to this changing landscape in order to run their practices as efficiently and effectively as possible and to provide the best care to their patients," said John Akscin, vice president of government relations and managed care services at OTN.

OTN provides oncology drugs, supportive care products and related supplies to more than 2, 400 office-based oncology practices in the US. Until May, OTN operated as a unit of Bristol-Myers Squibb Co. (NYSE: BMY). It was purchased by One Equity Partners LLC.

The amount of the OTN grant was not disclosed.

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Applied Biosystems (NYSE: ABI), an Applera Corp.business, of Foster City, Calif., said it has introduced its TaqMan Drug Metabolism Genotyping Assays for the detection and study of polymorphisms in the drug metabolism pathway.

The collection includes 2,000 assays of genetic variants in 220 genes that code for drug metabolism enzymes, the company said. A preliminary version of the assays is now available through an early-access customer program.

Gene variants or polymorphisms in drug metabolism enzymes play a role in altering drug concentration levels and determining side effect profiles of drugs for pharmaceutical biomarkers, the company said. Characterized polymorphisms provide a genetic basis for sample selection in clinical trials by differentiating study participants who could benefit from treatment from those who may experience adverse reactions.

Vanderbilt University and the University of Texas and Yale University are part of the TaqMan Drug Metabolism Genotyping Assays early access customers, the company said.

The TaqMan Drug Metabolism Genotyping Assays are single-tube probe and primer sets used with the Applied Biosystems real-time PCR instruments, including the 7300, 7500, and 7900HT Real-time PCR Systems, the company said. The assays can detect multiple types of polymorphisms, including single nucleotide polymorphisms, insertion/deletions, and multiple nucleotide polymorphisms, and have been limited to regulatory coding regions and splice junctions.

* * *

Genzyme Corp. (Nasdaq: GENZ) said it has created a test to detect low levels of disease, also known as minimal residual disease for B-cell chronic lymphocytic leukemia.

MRD refers to undetectable disease in the blood and bone marrow where complete remission has occurred, the company said.

A study in the Journal of Clinical Oncology indicated the elimination of disease to this extremely low level might improve the overall survival and treatment-

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free survival of B-cell chronic lymphocytic leukemia.

Eighty-four percent of patients who had no detectable CLL cells after receiving Campath had survived for at least 5 years, the study said. Twenty percent had failed to respond or had relapsed after receiving other chemotherapy for their disease. CLL patients who relapse from or are refractory to chemotherapy have the poorest prognosis with a median survival of 10 months.

The four-color flow cytometry test detects the presence of residual disease in the blood and bone marrow at far more sensitive levels than the light microscope or a bone marrow biopsy, which are used to detect leukemia, the company said.

The new technology can identify as few as one single CLL cell in 10,000 white blood cells. The test was based on a protocol developed by Leeds Teaching Hospitals in the U.K.

The test complements the Genzyme B-CLL treatment Campath (alemtuzumab), the company said.

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American Society of Hematology said it will participate in *patient*INFORM, an online service that provides consumers with the latest research on the diagnosis and treatment of certain diseases.

*patient*INFORM is a partnership between three voluntary health organizations and a group of scholarly and medical publishers that assists patients in understanding research findings published in several peer-reviewed biomedical journals.

Under the *patient*INFORM model, patients or their family members can visit the Web sites of the American Cancer Society (www.cancer.org), American Diabetes Association (www.diabetes.org), or American Heart Association (www.americanheart.org) to learn more about advances in treating specific diseases.

These organizations will provide consumers with links to the full text of selected journal articles as well as interpretation of the research that patients can apply to their own healthcare needs.

Through *patient*INFORM, ASH is making the full text of articles in *Blood*, its official journal, available to the participating voluntary health organizations as soon as each issue is published. Consumers will be provided with direct access to *Blood* articles on diseases such as leukemia, lymphoma, and myeloma.

During its initial pilot phase, *patient*INFORM will focus on cancer, diabetes, heart disease, and stroke. In the future, *patient*INFORM will extend its services to cover a wider range of medical conditions, the organizations said.

Product Approvals:

Mentor, FDA To Discuss Conditions For Approval

(Continued from page 1)

The conditions outlined in the approvable letter are generally consistent with the panel's deliberations, Mentor said. As is typical of FDA approvable processes, Mentor intends to engage in confidential discussions with the FDA to address these conditions, prior to the FDA's final decision on approval.

* * *

Ligand Pharmaceuticals Inc. (Nasdaq: LGNDE) of San Diego said it has received a letter from FDA requesting changes to the label of its sustained-release opiod product, Avinza, to strengthen warnings about alcohol consumption while using the treatment.

"In vitro observations indicate that the extended-release characteristics of Avinza are compromised in the presence of alcohol," said the FDA letter. "Until the clinical implications of these data are fully assessed, we request that changes be made to the package insert, with the intent to provide adequate information for the safe and effective use of the drug."

FDA also asked the company to send a "Dear Health Care Professional Letter" to inform of the label changes.

"The package insert carries several precautions about use of the product with alcohol," said James L'Italien, senior vice president for regulatory affairs and compliance for Ligand. "FDA suggested changes that would highlight and intensify warnings about alcohol intake while using Avinza. We're analyzing the request and are in dialogue with the agency.

"We may also need to do additional in vivo translational pharmacokinetic studies to assess which of the label changes or clarifications are ultimately appropriate," he said. "We intend to work with the FDA to effect agreed upon label changes and the Dear Health Care Professional Letter promptly."

Avinza, a once-a-day treatment for chronic moderate-to-severe pain when continuous, around-the-clock opioid therapy for an extended period of time is needed, was FDA approved in 2000, the company said. The drug consists of two components: an immediate-release component that achieves plateau morphine concentrations in plasma, and an extended-release component that maintains plasma concentrations throughout a 24-hour dosing interval.

Ligand co-promotes Avinza with Organon Pharmaceuticals USA Inc. in the U.S., the company

said.

* * *

OSI Pharmaceuticals Inc. (Nasdaq: OSIP) of Melville, N.Y., said Health Canada has approved Tarceva, erlotinib, for locally advanced or metastatic non-small cell lung cancer, following failure of first or second-line chemotherapy.

Tarceva, an oral tablet indicated for daily administration, is approved in the U.S. and in Switzerland and had received a positive opinion from the European Committee for Medicinal Products for Human Use, recommending approval for advanced NSCLC.

The Canadian approval indicates Tarceva as a monotherapy for locally advanced or metastatic non-small cell lung cancer after failure of at least one chemotherapy regimen, and where EGFR expression status is positive or unknown, the company said.

The 731-patient phase II study upon which the Canadian approval is based demonstrated that the treatment has a survival benefit in all subsets of patients examined including males and females, Asian and non-Asian origins, patients with adenocarcinoma and squamous cell histology, patients with good as well as impaired performance status and both smokers and non-smokers, the company said.

Median and one-year survival of the overall population in the BR.21 study was improved by 42.5 percent (6.7 versus 4.7 months) and 45 percent (31.2 versus 21.5 percent), respectively, and treatment with Tarceva for an average of just over four months (23 percent were on therapy for more than 6 months).

Certain subsets, including never smokers and those whose tumors were determined to be EGFR positive, were seen to have a large survival benefit. The sub- group of never-smokers had a substantial survival benefit with a hazard ratio of 0.42 (hazard ratio is a measure of the risk of death and a hazard ratio of <1 indicates a survival benefit). The sub-group of smokers also had a survival benefit (hazard ratio = 0.87) despite the fact that this group was also seen to have a 24 percent higher rate of Tarceva clearance (higher clearance rates lead to lower levels of exposure to drug), the company said.

In the NSCLC trial, common adverse reactions were rash and diarrhea, the company said. Grade 3/4 rash and diarrhea occurred in 9 and 6 percent, respectively. Rash and diarrhea each resulted in discontinuation of 1 percent. Dose reduction for rash and diarrhea was needed for 6 and 1 percent of patients, respectively.

Historically, there have been infrequent reports of serious interstitial lung disease, including fatalities, in with the drug for NSCLC or other advanced solid tumors. In the trial in NSCLC, severe pulmonary reactions, including cases of ILD, were infrequent (0.8 percent) and were equally distributed between treatment arms. The overall incidence of ILD in Tarceva-treated patients from all NSCLC studies was approximately 0.7 percent, the company said.

In another development, OSI Pharmaceuticals Inc. said FDA has accepted for filing and review the supplemental New Drug Application of Tarceva plus gemcitabine chemotherapy for advanced pancreatic cancer where no chemotherapy was administered.

The acceptance of the sNDA filing satisfies provisions for a $7 million milestone payment by Genentech Inc. to OSI, the company said.

* * *

Xillix Technologies Corp. (TSX: XLX) of Richmond, B.C., said U.S. FDA has given its consent for a pre-market approval supplement for Onco-LIFE, permitting commercial distribution in the U.S.

The technology is used with fluorescence imaging during bronchoscopy as an adjunct to white light imaging, in detecting and localizing tissue for moderate or severe dysplasia, carcinoma in situ, or invasive cancer where there has been suspected or previously treated lung cancer, the company said.

Xillix said it has appointed ConMed Endoscopic Technologies Inc., a division of ConMed Corp. (NASDAQ: CNMD) as the sole Onco-LIFE distributor for the lung cancer application in the U.S. and for both lung cancer and gastrointestinal application in Canada.

Onco-LIFE uses native tissue fluorescence to identify precancerous and cancerous tissue, the company said. Blue light is used to illuminate the tissue and excite fluorophors naturally present. A real-time video image of the fluorescing tissue is acquired and displayed on the video monitor, with areas suspicious for disease displayed in red in the video image enabling biopsy and further evaluation.

Clinical Trials:

Agensys Submits IND For Trial Of Monoclonal Antibody

Agensys Inc. of Santa Monica, Calif., said it has submitted an IND with FDA for a phase I trial of AGS-PSCA, a fully human monoclonal antibody for prostate, pancreatic, and bladder cancers.

The trial would focus on advanced prostate cancer, the company said.

AGS-PSCA is a high affinity, human IgG1k MAb

directed to the Agensys proprietary target Prostate Stem Cell Antigen, the company said. It was generated using XenoMouse technology through a licensing agreement with Abgenix (Nasdaq: ABGX).

"We are establishing a pipeline of human MAb products, targeted to our portfolio of proprietary cancer targets and we plan to file additional INDs as our programs continue to progress, said Donald Rice, chairman, president and CEO of Agensys.

"PSCA appears to affect both tumor cell growth and migration leading to a significant impact on all clinically relevant end points in xenograft models: tumor growth, metastasis formation, overall health, and prolongation of survival," said Aya Jakobovits, senior vice president, technology and corporate development and chief scientific officer. "In addition, enhanced activity is observed when it is combined with chemotherapeutic drugs."

* * *

AmpliMed of Tucson said it has begun enrollment in a phase I trial to evaluate Amplimexon injection in combination with dacarbazine for unresectable stage III or stage IV malignant melanoma where no chemotherapy has not been used.

Dacarbazine is a chemotherapeutic agent that interferes with cancer cell growth and is approved for sale in the U.S. as first line therapy for metastatic malignant melanoma, the company said. Data demonstrated the treatment increases the cytotoxic effects of DTIC on tumor cells in vitro and in animal models of melanoma tumor growth.

The trial, conducted at six centers of excellence in melanoma therapy across the U.S., would determine tolerance of the combination of Amplimexon and DTIC, followed by another enrollment to test the maximum tolerated dose of the combination for comparison with historical controls of DTIC alone, the company said. A randominzed trial would follow if positive results were seen.

Amplimexon avoids bone marrow toxicity and drug resistance and kills cancer cells by causing the disruption of mitochondria, resulting in the leakage of toxic substances, the company said.

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ARIAD Pharmaceuticals Inc. (Nasdaq: ARIA) of Cambridge, Mass., said it has begun enrollment for a phase II trial of mTOR inhibitor, AP23573, as a single agent for recurrent or persistent endometrial cancer.

The non-randomized 45-patient study would evaluate the clinical benefit of the inhibitor at centers in the U.S. and Europe, the company said. The dosage would be administered intravenously using a daily dosing regimen. Data on multiple mTOR-pathway biomarkers, including functional imaging in a subset of patients, would identify patients the most likely to benefit from the treatment, the company said.

* * *

AVAX Technologies Inc. (OTCMarket: AVXT. OB) of Philadelphia said enrollment has begun it a trial of M-Vax for stage III and IV melanoma.

The study multi-center trial would include up to seven clinical sites, the company said. In addition, a trial for metastatic peritoneal cancer has begun in France. Both studies would measure safety and include an immunological measure of vaccine activity as measured by delayed type hypersensitivity testing. The company said it has established a Data Safety Monitoring Board for the U.S. study.

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Celera Genomics (NYSE: CRA) of Rockville, Md., an Applera Corp. business, said it has begun phase I testing of its histone deacetylase inhibitor, CRA-024781, for refractory solid malignancies.

Samir Undevia, of the University of Chicago Hospitals in the Section, is conducting the 40-patient dose-escalation study for Hematology/Oncology, the company said. The objectives are to determine the maximum tolerated dose and to evaluate the safety and pharmacokinetics of the treatment.

CRA-024781 demonstrated efficacy an HDAC inhibitor in xenograft cancer models, the company said. In addition, it was demonstrated that the measurement of tubulin and histone acetylation can be used to monitor the pharmacodynamic effects of CRA-024781 in vivo.

* * *

Cylene Pharmaceuticals of San Diego said it has initiated a phase I trial for CX-3543, for multiple cancers.

The drug is a first-in-class small molecule with a mechanism of action that selectively induces apoptosis, the company said.

The trial is being conducted at the Cancer Therapy and Research Center in San Antonio, and at the Mayo Clinic, the company said.

The 36-patient trial for solid tumors or lymphomas, would determine the safety and tolerability of the product, characterize its pharmacokinetic profile, define dose-limiting toxicities and the maximum-tolerated dose, and select the appropriate dose for phase II trials, the company said.

CX-3543 is a proprietary small molecule, which selectively interacts with quadruplex nucleic acid

structures and induces apoptotic cell death in cancer cells, the company said. Preclinical studies have demonstrated favorable pharmacokinetic properties, potent in vivo efficacy in murine xenograft models with a broad safety window, as well as practical formulation, stability and drug manufacturing properties.

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Epeius Biotechnologies Corp.of Los Angeles said a phase I trial has opened at Mayo Clinic Cancer Center, for Rexin-G, a tumor-targeted gene therapy vector that has Orphan Drug designation from FDA for pancreatic cancer.

The clinical protocol has passed the reviews of FDA, the NIH/Recombinant Advisory Committee, and the Institutional Review Board of Mayo Clinic, the company said.

The dose-seeking 26-patient study would test the safety of increasing intravenous doses in advanced or metastatic pancreatic cancer when standard chemotherapy has failed, the company said.

Rexin-G contains a gene that blocks the action of the human cyclin G1 gene, a cell cycle control element. When injected into a vein, the treatment seeks out and accumulates in cancerous tumors, increasing the concentration of the drug in the cancerous tumors and not in normal other organs, the company said.

* * *

Infinity Pharmaceuticals Inc. of Cambridge, Mass., said it has begun a phase I trial of IPI-504, Heat Shock Protein 90 (Hsp90) inhibitor for multiple myeloma.

IPI-504 would also be developed for additional hematologic cancers and solid tumor indications, the company said.

The open-label safety assessment trial would evaluate the anti-tumor activity and the tolerability of various doses of relapsed or relapsed, refractory multiple myeloma, the company said. The trial is taking place at St. Vincent's Comprehensive Cancer Center in New York under the direction of Sundar Jagannath, chief of the Multiple Myeloma Service.

IPI-504 is a proprietary small molecule compound, the company said

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Infrared Sciences Corp. of Stony Brook, N.Y., said it has begun a clinical trial with **New York Presbyterian Hospital-Weill Medical College of Cornell University** of the Infrared Sciences Sentinel BreastScan imaging system for early breast cancer detection.

The system technology is based on advanced digital infrared imaging that is combined with software employing artificial intelligence techniques, the company said. Following the 4-minute test, it provides a fully-interpreted, objective report, the company said

The scan is an adjunctive procedure and does not replace mammography or ultrasound, or stand alone as a single test that can determine overall breast health, the company said.

* * *

Wilex AG of Munich, said it has completed its first phase I trial of the oral non-cytotoxic anti-cancer compound WX-671.

The open-label, single dose 16-patient study investigated the oral bio-availability, pharmacokinetics, and safety of the drug at four dose levels in healthy males, the company said.WX-671 was safe and well tolerated at all dose levels tested and did not lead to adverse events or other clinically relevant side effects. In addition, the compound showed good oral bio-availability, the company said.

WX-671 is a second generation serine protease inhibitor targeting the uPA (urokinase Plasminogen Activator) system, which has been shown to play a role in metastasis and primary tumor growth of breast cancer and other solid tumors, the company said.

WX-671 is an oral pro-drug of the Wilex investigational drug WX-UK1, which, in intravenous form, is being studied in cancer trials, the company said.. In pre-clinical models, WX-671 effectively blocked metastasis formation and primary tumor growth.

Deals & Collaborations:

Merck To Buy Rights To UFT From Taiho For Colon Cancer

Merck KGaA of Darmstadt, Germany, said it would acquire the global rights for UFT, tegafur-uracil, for colorectal cancer, from Taiho Pharmaceutical Co. Ltd. of Japan.

Taiho would supply the capsules to Merck for its territories and would retain rights in Japan, South Korea, Taiwan, Malaysia and Singapore, the company said.

UFT has marketing approval in 60 countries, would complement the Merck treatment for colorectal cancer, the monoclonal antibody Erbitux, the company said. Erbitux is approved in 39 countries.

"We see this as an excellent opportunity to extend our product portfolio in metastatic colorectal cancer," said Elmar Schnee, president of global ethical pharmaceuticals for Merck KGaA. "Our sales representatives are already discussing Erbitux with

oncologists who specialize in the treatment of gastro-intestinal cancers. Adding UFT to the discussion is a natural fit, even though Erbitux and UFT are intended for different stages of treatment."

UFT is an oral chemotherapy administered with folinic acid for first-line treatment of colorectal cancer that has metastasized, the company said. The drug shows comparable efficacy to intravenously administered 5-FU/FA, the mainstay treatment, and shows practically no disabling hand-foot syndrome.

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Cytyc Corp.(Nasdaq: CYTC) of Marlborough, Mass., said it has formed a partnership with Therapy System with Y-ME National Breast Cancer Organization in support of its MammoSite Radiation.

Y-ME, a patient advocacy group, would work with Cytyc on public education on less invasive treatment options for early-stage breast cancer, the company said. The program would include education on the benefits of partial breast irradiation and breast-conserving therapy. MammoSite Radiation Therapy, a form of partial breast irradiation, has been used at hundreds of U.S. centers.

The efficacy of the therapy is supported by the 2003 JNCI study that found that, over the course of five years, partial breast irradiation produces comparable results to whole-breast radiation therapy in preventing breast cancer recurrence in women with early-stage breast cancer who are treated with breast-conserving therapy.

To develop additional clinical data, the National Surgical Adjuvant Breast and Bowel Project and the Radiation Therapy Oncology Group, supported by NCI, began a multi-center study comparing whole breast irradiation with PBI over the long term.

The study would follow 3,000 women for 10 years to define the role of partial breast irradiation for the local management of early stage breast cancer, the company said.

* * *

GE Healthcare of Salt Lake City, a division of **General Electric Co.** (NYSE:GE), and **Intermountain Health Care** said they have entered into a collaboration to reduce medial errors by developing eMAR, an advanced electronic medication administration records center in West Valley, UT.

The clinical information technology would incorporate hand-held devices and bar-coding technologies, and would leverage in-depth clinical patient information to automatically validate and document prescribed medications, the companies said.

"Researchers and members of the medical community would work together to create new technologies that improve upon the current system of patient monitoring and enhance patient care by reducing errors that are the result of software that can quantify data, but isn't smart enough to qualify data," said Marc Probst, chief information officer of IHC.

* * *

Gene Logic Inc. (Nasdaq: GLGC) of Gaithersburg, Md., said it has signed an agreement with **GE Healthcare** (NYSE: GE) for global distribution of the Gene Logic Sciantis System, an online gene expression analysis system developed by academic, government and other non-profit research organizations.

GE Healthcare would distribute the system in 32 countries and would be the exclusive distributor in Japan, the company said.

The system is user friendly, browser based, and designed to profile the expression of human, rat and mouse genes in normal and diseased tissues to understand the relationship of gene expression to biological function and mechanisms of disease, the company said. Sciantis is based on the Gene Logic gene expression reference database, which allows accurate expression comparisons using the quality control metrics and sample processing automation of the company.

The features of the system include: 1) gene expression profiles from 6,000 human, rat, and mouse tissue samples curated by pathologists into 800 sample sets, 2) summary expression data for 30,000 genes in each sample set, 3) proprietary software that allows gene expression reports to be generated across a variety of cell lines or tissues, 4) data segmented into five disease areas, including inflammation, cardiovascular disease, oncology, central nervous system disorders, and metabolic diseases, the company said.

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Geron Corp. (Nasdaq: GERN) of Menlo Park, Calif., said it has entered into a collaboration and license agreement with **Merck & Co. Inc.** (NYSE: MRK) for cancer vaccine targeting telomerase.

Under the agreement, Geron said it would receive an upfront payment, milestone payments upon development and regulatory events, and royalties. Merck would acquire equity in Geron at a future date as part of the Geron next round of financing.

In addition, Merck has acquired an exclusive option to negotiate a separate agreement for the Geron dendritic cell-based telomerase vaccine in phase I/II trials at Duke University Medical Center, the company said. Geron would receive an option payment from

Merck in consideration for the option. The structure and terms of an agreement for the dendritic cell vaccine would be negotiated should Merck exercise its rights under the option, the company said.

* * *

Biopharmaceutical company **GroPep Limited** (ASX: GRO) said it has licensed certain Whey Growth Factor Extract technology rights to TGR BioSciences Pty Ltd. This arrangement will also allow TGR to raise additional funds to finance further development of the technology.

Under two separate agreements, venture capitalist Nanyang Innovation Fund managed by Nanyang Ventures will invest up to $3 million, TGR will start a clinical trial of WGFE for oral mucositis, and GroPep will license the WGFE technology to TGR.

GroPep will receive royalties of more than 10% from TGR on commercialization of the technology and TGR has taken over responsibility for five patent families developed by GroPep and the related costs. GroPep's shareholding in TGR is reduced from 20% to 12%.

Among the rights licensed to TGR is GroPep's oral mucositis product technology. Oral mucositis is a painful side effect afflicting chemotherapy patients. GroPep and collaborators have previously generated preclinical and clinical data, including a successful phase 1b trial conducted at the Peter MacCallum Cancer Centre in Melbourne, indicating the safety and potential for WGFE to treat this condition.

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Inovio Biomedical Corp. (AMEX: INO) of San Diego and **Vical Inc**. (Nasdaq: VICL) said they have begun a phase I study of gene-based IL-2 with Inovio electroporation technology for recurrent metastatic melanoma.

The method of delivering interleukin-2 protein is approved for metastatic melanoma, but causes severe systemic toxicities, the companies said. The treatment approach being studied directs injection into a tumor lesion of plasmid DNA encoding IL-2 followed by electroporation, the local application of electrical pulses, which enhance the uptake of the pDNA into tumor cells.

The pDNA cause cells within the tumor to produce high levels of IL-2 protein locally and stimulate the immune system to attack the tumor without the associated systemic toxicities, the companies said.

Treatments would be administered once a week in two four-week cycles, with each cycle followed by a four-week observation period, the companies said. The initial dose-escalation phase would enroll up to three patients each at doses of 0.5 mg, 1.5 mg and 5 mg delivered to a single tumor lesion per patient, with a final group receiving 5 mg in each of three tumor lesions per patient. Up to 17 additional patients would be treated at the highest tolerated dose. The primary endpoint in the trial is safety. Secondary efficacy endpoints would also be monitored.

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Odyssey Thera Inc. of San Ramon, Calif., said it has entered into an agreement with **Bristol Myers Squibb** to profile BMS compounds in the Odyssey Thera cell-based assays to characterize mechanism of action and pathway activity.

The protein-fragment complementation assay strategy allows for the on-pathway and off-pathway activities of compounds to be visualized and quantified in human cells, Odyssey said. Each assay reports on the sub-cellular activity of a compound at a particular node or branch of a biochemical pathway.

By testing a compound against a panel of assays, both intended and unintended activities can be identified and traced to a pathway and mechanism of action. The Odyssey Thera database of known drugs and toxic compounds allows a comparison of the activity of a compound with the activities of marketed and withdrawn agents and toxicants.

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ParAllele BioScience of South San Francisco and **Merck & Co. Inc**. said they have entered into an agreement to discover genetic variations in cancer.

Under the Merck-funded study, ParAllele would use its proprietary Single Nucleotide Polymorphism genotyping technology to characterize the genetic changes in tumor samples identified by Merck.

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SAS of Waltham, Mass., and **phase Forward** (NASDAQ: PFWD) of Cary, N.C., said they would integrate the phase Forward solution suite for clinical and safety data management with SAS Drug Development, a clinical trials data integration and analysis solution.

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Structural GenomiX Inc. of San Diego said it has extended its research and technology collaboration with **Eli Lilly and Co**. (NYSE: LLY) for three years.

Under the collaboration, SGX has applied its proprietary technologies to Lilly drug targets for high quality crystal structures and data on target/inhibitor complexes. Under a separate agreement, Lilly secured long-term access to the SGX synchrotron beamline facility to support structural chemistry programs.