THE CANCER LETTER

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Taking On Question Of Cost And Outcomes, CMS Turns To Expert In Cancer Care Quality

By Paul Goldberg

Soon after taking the top job at the Centers for Medicare and Medicaid Services, Mark McClellan set out to recruit a point man on quality of cancer care.

He offered the job to Peter Bach, an associate attending physician at Memorial Sloan-Kettering Cancer Center, a pulmonologist and critical care physician whose academic interests include epidemiology, biostatistics, and disparities in cancer care.

Last February, 40-year-old Bach took a leave from Memorial and

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In Brief:

GM Cancer Research Foundation Awards Annual Prizes To Brodie, Wogan, Kornberg

GENERAL MOTORS CANCER RESEARCH FOUNDATION has awarded its annual $250,000 prizes to three cancer researchers: **Angela Brodie**, **Gerald Wogan**, and **Roger Kornberg**. The scientists will receive the prizes at an awards gala in Washington, D.C., and will lecture at the foundation's annual scientific conference at NIH June 14-15.

Brodie, professor of pharmacology and experimental therapeutics at the University of Maryland School of Medicine and a University of Maryland Greenebaum Cancer Center researcher, won the Charles F. Kettering Prize for her pioneering work in developing aromatase inhibitors, a new class of drugs used to treat breast cancer. The Kettering Prize recognizes the most outstanding recent contribution to the diagnosis or treatment of cancer.

Brodie began developing the novel approach of targeting aromatase in the early 1970s, initially working with her husband, Harry, who synthesized the early inhibitors. Brodie and her research team went on to create the first selective aromatase inhibitor to be used to treat breast cancer patients. Released for worldwide use in 1994, the drug, Formestane (4- hydroxyandrostenedione), was the first new compound in a decade specifically designed for the treatment of breast cancer. Her work paved the way for the development of other aromatase inhibitors, three of which have been approved by FDA for the treatment of breast cancer. She has expanded her research into prostate cancer and is now developing steroidal compounds that target key enzymes in the production of androgens which play a role in recurrence of the cancer.

Wogan, a senior research fellow in the NCI Laboratory of Human

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Peter Bach Becomes In-House Cancer Quality Expert At CMS

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accepted the job at the federal agency. His move makes CMS-watchers wonder whether the addition of an enthusiastic, number-crunching doctor to McClellan's staff can alter the agency as it expands its mission to demanding improvements in the quality of medical care.

Even McClellan's decision to create the position of a "senior advisor to the administrator" on cancer health care quality is viewed as symbolic.

"The message I get is that the assessment of quality in cancer care has lagged behind other areas," said Rodger Winn, project director for cancer quality assessment at the National Quality Forum, a non-profit group that evaluates and endorses quality standards for the agency.

"I think CMS recognizes that cancer is a major portion of their budget, and therefore, they are going to have to come to grips with how to deal with it," Winn said. "This is a way for CMS to ensure that they have an in-house cancer expert."

"I view Dr. McClellan's appointment of Dr. Bach as consistent with his dedication to improving the quality of cancer care," said Ellen Stovall, president and CEO of the National Coalition for Cancer Survivorship. "Dr. Bach's outreach to the clinical oncology community and groups like ours sends a strong signal that CMS is seeking guidance from those who will benefit most from quality improvement initiatives—cancer patients themselves."

Bach describes his job as "an opportunity of a lifetime," a chance to apply what he learned in the clinic and through his work in health services research. "I have been studying the health care system, observing it, being part of its inefficiencies, trying to provide high quality care despite systemic barriers."

The decision to move to CMS was simple, Bach said. "The only issues for me were logistical ones, like can I do it and maintain my family life?" he said. Bach, who lives in Brooklyn, now spends two or three days a week working in the Washington office, and the rest of the week at the agency's offices in New York.

Setting the Bar for Payment

McClellan became the CMS Administrator at a time when the agency has to devise a strategy for paying for the new generation of cancer drugs and biologics that can extend survival, but run up six-figure bills for a year of therapy.

The agency has never had an in-house expertise in oncology, and in battles past, oncologists ended up dealing with CMS officials who had to be walked through data slowly and deliberately.

"It's important to have a cancer expert in the inner sanctum at CMS," said Richard Goldberg, professor and chief of the division of hematology and oncology at the University of North Carolina Lineberger Comprehensive Cancer Center. Two years ago, Goldberg presented data to CMS and found that decisions were being made by people who lacked familiarity with cancer treatment.

Another agency, the Food and Drug Administration, has become easier to deal with after it hired an academic oncologist to run its cancer programs, Goldberg said. "Look at what it has done to have [oncologist Richard] Pazdur at FDA," said Goldberg, referring to the director of the FDA Division of Oncology Drug Products who was recently named director of the Office of Oncology Drug Products. "There is a clinical trialist who understands what it's like to be in the clinic. He has been a real help to patients and the oncology world. If we can have somebody who is coming from a good background in a position like that at CMS, it will only help us."

An argument can be made that the biggest challenge faced by CMS begins at the doors of FDA. The drug approval process is based on safety and efficacy. Comparisons of therapies are usually kept to a minimum, and cost-effectiveness isn't addressed.

Many questions, including pinpointing optimal

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treatments—or the optimal duration of treatments—require randomized clinical trials. Yet, CMS doesn't have a clinical trials network and cannot sponsor trials or mandate that trials be conducted either by NCI or by pharmaceutical companies.

Over the years, the FDA approval of a drug meant that CMS would pay for the approved indication and some off-label uses. Two years ago, CMS broke with tradition by starting a "national coverage analysis" of Eloxatin (oxaliplatin), in part because of its "impact" on Medicare (The Cancer Letter, March 21, 2003).

The stakes were enormous. Had the agency issued a negative decision on the drug, the CMS regional carriers would have been precluded from paying for it.

"With that request, CMS sent a message to the pharmaceutical industry, saying that in the future, FDA approval might not be the final hurdle and that additional criteria, set by CMS, would need to be cleared in order to warrant coverage," said Mace Rothenberg, Ingram Professor of Cancer Research at Vanderbilt-Ingram Cancer Center and one of the principal investigators in the Eloxatin trials.

The agency's criteria for payment seemed unclear.

"We knew, based on years of experience, what the criteria are that FDA have based their decisions on in the past," Rothenberg said. "You have the transcripts, you have the videos, you get a chance to hear their thinking in a public forum. That didn't seem to occur, or not be required, at CMS."

To make a case before the agency two years ago, Rothenberg and Goldberg prepared a scientific presentation calibrated for non-specialists. "They were all physicians, and they obviously can read the literature, but you certainly would want to interact with someone who has a lot more than just a short review under their belt in order to make such an important decision as national coverage for new and very expensive agents," Rothenberg said.

"I would say they were eager and alert, but they were rheumatologists and neurologists, and people who really had no clinical exposure to the sorts of things that they were being asked to make decisions about," Goldberg recalled. "It was hard to get a sense that they understood the issues as well as you would have liked. None of them revealed a depth of knowledge in their questions or in their discussion. You were forced to be respectful because they had you in their vise."

The agency's coverage analysis started with Eloxatin, but expanded to include Camptosar (irinotecan), Erbitux (cetuximab), and Avastin (bevacizumab). Now, the entire new generation of colorectal cancer therapies was at risk.

McClellan moved over from his job as FDA Commissioner to take over CMS in February 2004. In oncology, he needed to find a resolution to the lingering coverage analysis on colorectal cancer treatments and redraw the schema for reimbursement of office-based oncologists. He approached both problems with a similar strategy, offering payment in exchange for data.

On Nov. 3, 2004, literally the day before the elections, CMS added $300 million as payment for oncologists to collect data in a one-year demonstration project to study side effects of cancer therapy (The Cancer Letter, Nov. 5, 2004).

On Jan. 28, the agency decided to reimburse experimental use of the colorectal cancer drugs in the context of nine NCI-sponsored trials. The agency will continue to pay for the agents' approved uses as well as for off-label uses supported by medical literature.

Recently, CMS solidified this principle in a draft guidance on providing "coverage with evidence development," a category of payment that would allow reimbursement contingent on collection of data. The document is available at www.cms.hhs.gov/coverage/guidance.asp.

Health & Policy

Like McClellan, who is a physician and an economist, Bach has been interested in clinical medicine and the health care delivery system.

The son of a transplant immunologist and cancer geneticist father and biochemist mother, as an undergraduate at Harvard, Bach meandered between pre-med courses, mathematics, and English and American literature. After taking two years to teach English in prep schools, he went into medicine.

As a resident at Johns Hopkins Hospital, Bach became interested in drug addiction, which triggered an interest in health disparities, health policy, and the structure of markets for illegal drugs.

"When I was at Hopkins, I saw what everyone there sees, which was a disconnect between what is done in the acute care setting to treat manifestations of disease and what is done in the outpatient setting to prevent illness," he said. "The greatest amount of preventable illness I saw working on the wards at Hopkins, in East Baltimore, was due to drug use. It seemed like something that was so preventable.

"I watched people who were addicted to heroin get discharged and come right back. There was absolutely no infrastructure to support them after they were

discharged. That got my attention. We have a healthcare system that had walls built around it, and they perfectly paralleled the brick walls of the hospital itself. That didn't make much sense to me."

Pursuing these interests as a Robert Wood Johnson Clinical Scholar at the University of Chicago, Bach found himself on parallel tracks, studying both the heroin problem and pulmonary and critical care.

He first focused on lung cancer as a pulmonologist, then as an epidemiologist. "Lung cancer is vastly preventable, and it's a disease that has interesting other features," he said. "It disproportionately affects poor people. It disproportionately affects African Americans. It's a disease that, if you catch it early, is highly treatable. There are many aspects of the system and the social parts, and the early detection aspect of it that drew me toward lung cancer."

Bach's first job after fellowship was at Memorial Sloan-Kettering Cancer Center, where he joined the departments of medicine and epidemiology and biostatistics. At Memorial, he continued to study the differences in health care received by blacks and whites.

Using data on Medicare patients, Bach showed that black patients were less likely than whites to receive surgery for early-stage lung cancer, and that difference was sufficient to account for the difference in survival. "It was a miniscule piece of the puzzle, but it ties together the things that I've been focusing on, which were social determinants of health care quality," he said.

In another paper, Bach showed that black patients receive care from a subgroup of physicians whose qualifications and resources are inferior to those who treat white patients. In another, he showed that patients who get lung cancer surgery at hospitals that perform a higher volume of such procedures are less likely to die of postoperative complications.

"We were figuring out stuff from data that we got our hands on that was created for another purpose," Bach said. "I've heard from the cancer community concerns that coverage under evidence development or coverage in the context of registry creation is just a bad idea, because you can't figure out anything from observational data. I have carved a career out of figuring out stuff from observational data. If you gather information in a systematic way about people who are being treated in a particular way, there are things you can figure out about treatments themselves."

Bach said he first met McClellan about four years ago, and the two exchanged emails on research topics.

The job offer came up in a series of conversations in late fall of 2004, Bach said. "We were talking about the issues in cancer and the CMS role in promoting high quality care," Bach said. "My entire research career has been focused on trying to understand, and measure, and improve health care quality. Dr. McClellan was moving CMS toward doing just that in an applied way."

"The Right Care For The Right Patient"

What is quality?

"The correct answer is that it's the right care for the right patient every time," Bach said. "It's a slogan, but it's the right matching of therapies and devices and aggressiveness and palliation with the patient. That is literally only something that can be decided at an individual level between doctors and patients."

The absence of quality may be easier to recognize than its presence, Bach said. "We have an avalanche of research suggesting that, although an individual treatment decision may be hard to second-guess, if you look in the aggregate, many of these decisions are not the highest quality for patients," Bach said.

"Not all patients are getting beta-blockers after heart attacks. Some of them shouldn't, but not the numbers we see. And patients aren't getting adjuvant therapy for colon cancer. Some of them shouldn't, but the numbers not getting adjuvant therapy doesn't jive with anything we know about the population that gets colon cancer. Patients aren't getting lung cancer surgery as frequently as they should, and it explains the racial gap in lung cancer survival.

"We are going to figure out how to measure quality at the most granular level. And we are going to have to figure out how to create a system that's better for doctors, so they can achieve quality. That will require modernization of the payment system."

The reimbursement system doesn't encourage quality cancer care, Bach said. Doctors are paid exclusively for discharging services without regard for outcomes, which guarantees that a lot of services will be provided and a lot of resources consumed.

"Part of the growth in expenditures for cancer care is due to inefficiencies in the system," Bach said. "How are we going to pay for the new generation of therapies that clearly benefit patients? We are going to have to find a way if it's benefiting patients. We need to do a really good job of paying for things that benefit patients a lot, and try to work some of the inefficiencies out of the system, where patients are not benefited at all, and often harmed. For example, getting too many CAT scans. Patients are getting CAT scans because doctors can't find

the old CAT scans, and because the indications for CAT scan and other imaging tests are not well defined.

"The estimates are all over the map, but they are pretty sizable, that a lot of what we have in the system is waste."

Demonstration Project To Yield Useful Data

Bach said the chemotherapy side effects demonstration project shows that it is possible for Medicare to collect data through the billing system.

Doctors who take part in the project are paid to administer a questionnaire to patients each time they provide chemotherapy. Patients are asked to rate the severity of nausea and vomiting, fatigue, and pain they experience at the time of treatment, and their answers are assigned billing codes.

"We are going to know about hundreds of thousands of cancer patients and their levels of nausea, vomiting, fatigue, and pain while they are getting chemotherapy in 2005 in the U.S.," Bach said. "It's going to tell us whether we are where we need to be with nausea and vomiting control, where there has been major pharmacologic progress. We will know where we are in terms of pain control. We will know where we are in terms of fatigue.

"It's observational data, collected on thousands and thousands of patients across the country, using claims," Bach said. "That's exactly what my research focuses on."

Winn agrees that the data would be useful. "The exciting thing about that is that you have a mechanism in place to collect data, linked to Medicare records," he said. "It's a proof of concept that you can do it. Now, the question is whether you can generate quality questions that are really important."

While some questions can be answered with observational data gleaned from the billing system, others require nothing less than randomized clinical trials.

Comparisons of safety and efficacy of treatment regimens become all the more complicated when questions of cost-effectiveness are thrown into the mix, clinical trialists say.

"Right now, it doesn't seem like there are any guidelines that CMS or even insurance companies are using for guiding coverage," said Rothenberg. "It has been left up to the decision of the physician and patient, and in a sense, that's the way it should be. But in another sense, should economic impact factor into a decision? For instance, continuing Avastin second-line after a first-line Avastin-containing regimen fails. Some people are doing that. We have no data whatsoever to support that use. But should it be covered? I don't know. There is no data for that, so I don't do it."

Recently, Goldberg was surprised by NCI's refusal to fund the economic and quality of life analysis in a trial of Avastin, Erbitux, or both, in conjunction with chemotherapy in first-line treatment of advanced colorectal cancer.

The trial—Cancer and Leukemia Group B study 80405—is conducted by the Gastrointestinal Cancer Intergroup.

"We have made a lot of recent progress in managing colorectal cancer, but each of these advances has led to an order of magnitude increase in the expense for palliative treatment," said Goldberg, chairman of the CALGB GI committee and the GI Intergroup's colon cancer task force. "One would think that the government, which pays for the medical care of most colon cancer patients, would be eager to obtain and willing to underwrite an effort to collect objective data to help us all make judgments about the value and the costs of these new treatments."

CALGB Chairman Richard Schilsky said the quality of life and economic analysis was essential to the study.

"Clearly, the CALGB and SWOG investigators believe these studies are important or we wouldn't have proposed them to begin with," Schilsky said. "If the primary objective of the trial is met, i.e., that cetuximab improves survival when added to chemotherapy plus bevacizumab in first-line treatment of metastatic colorectal cancer, it will be important to understand the societal consequences of this advance in economic and quality of life terms. Despite NCI's unwillingness to support these studies, they have been retained in the protocol and will be supported with non-federal funds."

Calculated at the average wholesale price minus five percent, a year's worth of drugs used in one of the trial's four arms—Avastin, Erbitux, Eloxatin, 5-fluorouracil and leucovorin—for a hypothetical patient with the body surface of 2 m^2 would cost $297,604.

International News:

Charities Slow To Address Increase In Pediatric Cancer

The emergence of cancer as a major cause of death among children in developing regions of the world is not being adequately addressed by national or international health organizations and charities, according to

investigators at St. Jude Children's Research Hospital. This growing rate of pediatric cancer is occurring as the number of children dying from infectious diseases is being reduced through the efforts of the World Health Organization and international charities, the researchers say.

Healthcare organizations and charities have traditionally focused on relatively inexpensive strategies for combating infectious diseases, said Ching-Hon Pui, director of the Leukemia/Lymphoma Division at St. Jude, and American Cancer Society F.M. Kirby Clinical Research Professor. This decision has left many children with cancer in much of the developing regions of Asia, South and Central America, Africa, and the Middle East without access to effective medical treatment. Pui is a co-author of an editorial on the geographical inequality of pediatric cancer treatment that appears in the May 26 issue of the New England Journal of Medicine.

"More than 60 percent of the world's children have little or no access to effective cancer therapy," said Pui. "And their survival rates are very inferior to rates in countries with advanced health care systems. However, the World Health Organization and many international charities don't even list chronic diseases, including cancer, as health priorities on their agendas."

The increasing pediatric cancer death rate in countries with limited resources is especially tragic, because there are strategies that can be used to ensure wider access to effective cancer treatment, according to Raul Ribeiro, director of the International Outreach Program at St. Jude and another co-author of the editorial. The authors note that one of the most effective strategies is a cooperative process between institutions, called twinning, which is already in place in Central and South America, Africa, and Southeast Asia, through the International Society of Pediatric Oncology, several institutions in Europe, and St. Jude.

"We've found that recruiting local oncologists to serve as program directors gives the best results," said Ribeiro. "The recruited oncologists serve as program directors, advocates of pediatric oncology units, and coordinators of training for essential cancer care providers."

The authors argue that even the very low level of development that exists in some parts of the world is not an insurmountable obstacle to establishing a productive twinning relationship. A program that concentrates on education, training, and the treatment of the most responsive cancers could be effective, they said. For example, in parts of Africa it might be possible to successfully treat children who have Burkitt's lymphoma using a single drug, cyclophosphamide. Such twinning projects can be supported initially by the partner in the more affluent country, the authors said. Over time, local fundraising by charitable groups can raise money to support the oncology program.

Another benefit of twinning would be broadening of the scope of cancer research to include cases in developing countries, the authors note. This would facilitate studies of the roles that genetic background, environment, and lifestyle play in susceptibility to cancer and pathogenesis of particular cancers. Such studies will be easier to do if pediatric cancer units are created in resource-poor nations, and if their development promotes international cell and tissue banks and the ability to collect long-term treatment follow-up data.

Funding Opportunities:

Program Announcement

PA-05-116: Pilot Studies in Pancreatic Cancer

Letter of Intent Receipt Dates: http://grants.nih.gov/grants/funding/submissionschedule.htm. Application Receipt Dates: http://grants.nih.gov/grants/funding/submissionschedule.htm

Through this PA, NCI is promoting R03 and R21 research across multiple disciplines for the biology, etiology, detection, prevention, and treatment of pancreatic cancer. Examples of appropriate research areas include, but are not limited to: Identification of genetic aberrations (e.g., mutations, epigenetic changes, etc.) or combinations of aberrations alterations that initiate or promote pancreatic cancer; Development of experimental models for human pancreatic cancer to facilitate the understanding of molecular carcinogenesis, to help to identify promising molecular targets, and to test new preventive/therapeutic strategies; Exploration of molecular pathways using human cell lines and/or tissues to identify possible novel targets for prevention or therapeutic development; Identification of markers for early detection of cancer; Conduct of preclinical studies to identify candidate chemopreventive drug(s) and dietary factors for prevention and to characterize the molecular mechanism(s) of the agent's activity; Conduct of small exploratory clinical trials with a potential chemopreventive agent (e.g., a farnesyltransferase inhibitor or a statin) assessing response via endoscopic ultrasound or another similar technology; Development of early-stage clinical trials in pancreatic cancer prevention and therapy; Assessment of any associations of tumor pathophysiology on tumor development, progression, and preventive/therapeutic response; Conduct of exploratory studies to identify and evaluate biomarkers (with associated assay development) to determine prognosis and predict response to therapy in pancreatic cancer; Evaluation of combination therapies for pancreatic cancer; Identification of new environmental exposures (e.g., adverse energy balance) that may contribute to pancreatic cancer development,

including adverse energy balance; Assessment of the impact of pancreatic cancer on health-related quality of life of patients and their caregivers; and conduct of pilot surveillance studies and generation of survivorship registries. The PA is available at http://grants.nih.gov/grants/guide/pa-files/PA-05-116.html.

Inquiries: For cancer control, epidemiology, and survivorship: Mukesh Verma, Division of Cancer Control and Population Sciences, phone 301-594-7344; e-mail vermam@mail.nih.gov. For cancer biology and models: Judy Mietz, Division of Cancer Biology; phone 301-496-9326; e-mail mietzj@mail.nih.gov. For cancer etiology: Mary Ellen Perry, Division of Cancer Biology; phone 301-496-7028; e-mail perryma@mail.nih.gov.

For cancer exogenous factors including diet and cancer prevention: Sharon Ross, Division of Cancer Prevention, phone 301-496-8573; e-mail rosssha@mail.nih.gov. For cancer diagnosis and treatment**:** Roy Wu, Division of Cancer Treatment and Diagnosis; phone 301-496-8866; e-mail wur@ctep.nci.nih.gov.

Extension of Bioengineering Nanotechnology Initiative SBIR PA-02-125: Applicants should note that the PA for the Bioengineering Nanotechnology Initiative at http://grants.nih.gov/grants/guide/pa-files/PA-02-125.html will remain active for one additional receipt date: Aug.1, 2005, and that new application forms are required.

Inquires: Jeffery Schloss, program director, Technology Development Coordination, National Human Genome Research Institute, phone 301-496-7531; e-mail jeff_schloss@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 interdisciplinary studies held by Westat Inc. to conduct a wide variety of domestic and international family studies and field (case-control and cohort) studies. Major activities of the contract provide: 1) nursing support including contacting family members, explaining the studies, enrolling family members, obtaining clinical information and records, requesting pathology slides for diagnosis confirmation, arranging for family members to be evaluated by GEB investigators in the Cancer Genetics Clinic at the Clinical Center, performing phlebotomy, obtaining other biologic specimens as necessary, arranging and conducting field trips to evaluate family members, verifying information for the family registry database, maintaining tracking systems for data and biologic specimens, developing and providing educational materials for participants, and participating in genetic counseling and risk notification; 2) maintenance of a locked medical record room to which GEB investigators have immediate access; 3) development of coordination and liaison at a local or international level with collaborating investigators or institutions whose cooperation is needed for the conduct of a study; 4) assistance in the design and pilot testing of forms required for field investigations (e.g., questionnaires, abstracting forms, coding forms, manuals for field procedures and other documents); 5) hiring, training and supervision of field personnel (interviewers, abstractors, and others); 6) identification of study subjects, including locating cancer patients and/or their relatives, selection of controls through such methods as random digit dialing and acquisition of appropriate study population rosters or files; 7) supervision and management of field operations; 8) collections of data (interviewing/record abstraction, biologic specimen collection and processing); 9) data reduction activities (coding, keying, and editing) of data collected into a format suitable for computer analysis; 10) quality control and standardization so that appropriate and valid data result. The RFP is available at http://rcb.cancer.gov/rcb-internet/.

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In Brief:

Brodie, Wogan, Kornberg Win GM Foundation Prizes

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Carcinogenesis and the emeritus Underwood-Prescott Professor of Toxicology and professor of chemistry at the Massachusetts Institute of Technology, won the Charles S. Mott Prize for his research on mechanisms of toxicity, especially carcinogenicity and mutagenicity. The Mott prize honors an outstanding contribution relating to the cause or prevention of cancer.

Wogan, a pioneer of environmental toxicology, has led a long-term effort to describe the fundamentals of chemical carcinogenesis. His research has emphasized understanding the chemistry and toxicology of aflatoxins, using synthetic and structure-activity studies to demonstrate the utility of chemical approaches in understanding mechanisms of toxicity. His studies showed that aflatoxin is a risk factor in the etiology of hepatocellular carcinoma.

Kornberg, professor of structural biology at Stanford University, will receive the Alfred P. Sloan Jr. Prize for his pioneering research in the field of transcription. The Sloan prize recognizes outstanding basic science research.

Kornberg discovered and described in detail the nucleosome, which controls the expression of genetic information encoded in DNA. This research influenced later work on the structure of chromatin and its role in gene regulation. His research has focused on the enzyme RNA polymerase, which was discovered by

Robert Roeder, a previous Sloan prize winner. Kornberg described the three-dimensional structure of RNA polymerase.

* * *

JAMES MULSHINE, head of the Experimental Intervention Section in the Cell and Cancer Biology Branch, NCI Center for Cancer Research, plans to leave the Institute on July 16 to take a position as associate provost for research at Rush University Medical School, Chicago. Mulshine, who conducts research in lung cancer prevention, graduated from the Loyola Stritch School of Medicine in 1977, completed a fellowship in internal medicine, and was a resident at the Cleveland Clinic Foundation. He completed his training in medical oncology and spent nine years in the NCI-Navy Medical Oncology Branch. In 1990, he moved to the Division of Cancer Prevention and Control to start an Intramural Translation Research Group that was moved back to the Division of Clinical Sciences in 1996. After moving to Rush, he will become a full voting member of the board of the Lung Cancer Alliance, where he has served as a non-voting member. . . . **LUNG CANCER ALLIANCE** selected three new board members: **Priscilla Dewey Houghton**, lung cancer survivor and wife of Amo Houghton (R-NY), **Cheryl Healton**, president and CEO of the American Legacy Foundation, and **Harvey Pass**, professor of surgery and oncology at Wayne State University, and chief of thoracic oncology at Karmanos Cancer Institute. The new slate replaces **Margaret McCarthy**, founder of the Lung Cancer Alliance (formerly ALCASE), **Randy Urmston**, lung cancer survivor and attorney in Seattle, and James Asher, lung cancer survivor and former executive director of ALCASE. . . . **MARY TODD**, professor of medicine at UMDNJ-Robert Wood Johnson Medical School, was appointed chief medical and operating officer of the Cancer Institute of New Jersey, coordinating all administrative and financial activities of the NCI-designated comprehensive cancer center, said **William Hait**, center director. **Arnold Rabson**, professor of molecular genetics at UMDNJ- Robert Wood Johnson Medical School, was appointed deputy director of the center. He will oversee the center's scientific research and laboratory functions. **Eileen White**, professor of biological sciences at Rutgers University, was named associate director for basic science. The center also has established the C.R. Bard Urology Scholars Program with a $10,000 grant from the C.R. Bard Foundation. The program will provide medical students access to urologic oncology research to increase the number of students who choose urologic oncology as a specialty. Two medical students will be trained in clinical and laboratory aspects of urology. Each student will be paired with a clinical mentor, as well as a research mentor and will spend the majority of his/her time in the laboratory. Students will also spend about one-half day per week with their clinical mentor in the outpatient clinic, ward rounds, and operating room. . . . **CAROL KELLY** was appointed head of the new Office of Policy at CMS as of June 13. Kelly was a lobbyist at AvaMed. . . . **JAMES CHINGOS** was named chief of the Division of Hematology-Oncology, Department of Medicine, University of Florida at Jacksonville. He also was appointed associate director of clinical affairs for the UF Shands Cancer Center. He was medical director of the Cape and Islands Regional Cancer Center at the Davenport-Mugar Cancer Center in Hyannis, Mass. . . . **CRAIG THOMPSON**, scientific director of the Abramson Family Cancer Research Institute and deputy director of the Abramson Cancer Center of the University of Pennsylvania, was elected to the National Academy of Sciences. He also is chairman of the Department of Cancer Biology at the UP School of Medicine. . . . **PURDUE UNIVERSITY** received a $6.8 million, five-year grant from NCI for cancer research into natural cancer preventatives derived from land- and ocean-dwelling organisms. The grant is a renewal of one given in 1991 to **John Pezzuto**, professor of medicinal chemistry and molecular pharmacology and dean of the College of Pharmacy, Nursing and Health Sciences at Purdue, and his team. The initiative includes the participation of a multidisciplinary group from the University of Illinois at Chicago, Scripps Institute of Oceanography and Purdue. "Our team has located many active natural substances that could be used to treat colon, skin and breast cancer," said Pezzuto. "We have nine patents and two drug development programs that derive specifically from the work we have done. One is Resveratrol, one of the most promising substances the group has found. Deriving from a Peruvian plant, the substance could treat viruses, heart disease, Alzheimer's disease, as well as cancer. Deguelin, another substance from Zimbabwe, is being studied for lung cancer, skin and breast cancer, said Pezzuto. Several separate projects for chemoprevention, are to be funded by the grant. "Chemoprevention gives people non-toxic substances that can be consumed orally and that will help stave off cancer," Pezzuto said. "The team prepares extracts and evaluates them with a panel of tests that indicate how well each material inhibits major stages of carcinogenesis. The tests have been explicitly designed for this purpose, Pezzuto said.

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

Product Approvals & Applications:

Amgen Submits sBLA For Aranesp Based On Phase III Trial In Kidney Cancer

Amgen Inc. (Nasdaq:AMGN) of Thousand Oaks, Calif., said it has submitted a supplemental biologics license application for Aranesp, darbepoetin alfa.

The sBLA is based on phase III data that will demonstrate that Aranesp administered every three weeks is safe and effective for chemotherapy-induced anemia in non-myeloid malignancies.

Aranesp, a erythropoiesis stimulating protein, contains two additional sialic acid-containing carbohydrate chains than the Epoetin alfa molecule

(Continued to page 2)

Deals & Collaborations:

Starr Foundation Provides Initial Funding For Tri-Institutional Stem Cell Initiative

Rockefeller University, **Weill Medical College of Cornell University**, and **Sloan-Kettering Cancer Center** said they have received $10 million of the $50 million three-year award from The Starr Foundation of New York to form the Tri-Institutional Stem Cell Initiative.

The gift will enable the hiring of scientists, the training of leaders in stem cell research, and the development shared facilities for stem cell lines and expansion and maintenance of existing cell lines, the institutions said.

Emphasis will be placed on collaborative studies bringing stem cell researchers together with colleagues from other fields including neuroscience, cell cycle research, toxicology, chemistry, and physics.

By including human embryonic stem cells—both those registered by the federal government and those that are not—along with adult stem cells and stem cells from cancers and experimental animals, the initiative would ensure access to the most appropriate, robust cell line for study, the institutions said.

The broad approach would allow exploration of biological significance of stem cells and comparison of the relative merits of all cell lines in terms of their function and therapeutic potential, the institutions said.

"Bringing together the complementary strengths of our three institutions will ensure that we continue to pursue the highest quality research and use the knowledge we gain for the betterment of human health," said Antonio Gotto Jr., the Stephen and Suzanne Weiss dean of Weill Cornell Medical College

(Continued to page 6)

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Celera Genomics Submits IND To FDA For HDAC Inhibitor

(Continued from page 1)

and remains in the bloodstream longer than Epoetin alfa, because it has a longer half-life. By virtue of its longer half-life, the protein should be administered less frequently than Epoetin alfa for chronic kidney disease, the company said.

* * *

Celera Genomics (NYSE:CRA) of Rockville, Md., said it has submitted an IND application to FDA for CRA-024781, a histone deacetylase inhibitor.

Data demonstrates the efficacy of CRA-024781 as 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 the inhibitor in vivo.

HDAC enzyme inhibition causes changes to chromatin structure and to gene expression patterns, which results in the inhibition of proliferation of cancer cells, and induction of apoptosis, the company said.

* * *

CeMines Inc. of Golden, Colo., said it has filed a 510(k) application with FDA, seeking clearance for clinical use of its cancer detection kit, the CeMines CellCorrect LAb.

The test detects altered autoimmunity and associated patterns of disease-related autoantibodies in the bloodstream, the company said. Clinical studies demonstrated that specific and consistent patterns of antibodies have regularly proven their utility as composite biomarkers to characterize cancer, and can be used as diagnostic tests for cancer. The company said it uses a proprietary bioinformatics-based statistical pattern recognition application, CeMines Molecular FingerPrinting, that evaluates patterns of certain antibodies and the profiles of cancer patients. These data are presented to assist physicians in diagnosis of cancer.

* * *

Curis Inc. (NASDAQ:CRIS) of Cambridge, Mass., said that an IND application filed by its collaborator **Genentech Inc**. (NYSE:DNA) has been accepted by FDA to initiate a clinical trial for the topical treatment of basal cell carcinoma.

The drug candidate is an antagonist of the Hedgehog signaling pathway that was discovered by Curis and is being co-developed through a collaboration between Genentech and Curis, the company said.

* * *

Northwest Biotherapeutics (OTCBB: NWBT.OB) said it received FDA clearance to begin assessment of its dendritic cell-based product candidate, DCVax-Brain, in a phase II clinical trial with approximately 150 patients at 12-15 sites in the U.S.

DCVax-Brain is a personalized vaccine that is made from a patient's own dendritic cells and mobilizes the patient's immune system to attack his or her brain cancer.

The phase II trial is based upon promising clinical data from two phase I clinical trials carried out at University of California, Los Angeles, by Linda Liau, in patients with Glioblastoma multiforme (GBM), the most lethal form of brain cancer. In these trials, a total of 25 patients were treated with DCVax -Brain. Seventeen of these were newly diagnosed GBM patients, and eight were recurrent GBM patients.

DCVax-Brain delivered substantial delays in the time to disease progression and substantial extension of survival times in both groups of patients, compared with the standard of care treatment for such patients, the company said. The improvements in time to progression and survival time were significant for both groups of patients, but were larger for newly diagnosed patients than for patients with later stage recurrent disease.

With existing standard of care treatment, newly diagnosed GBM patients historically have a median time to disease progression of eight months and median survival of only 15 months. With DCVax-Brain, the

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newly diagnosed patients in the two phase I trials have a median time to progression of 15 months and median survival time in excess of 26 months. No material toxicity was seen in any of the patients.

Recurrent GBM patients have an even bleaker prognosis with existing standard of care treatment. Historically, their median time to disease progression is only 5 months, and median survival is only 10 months. With DCVax-Brain, the recurrent GBM patients in the phase I trial show a median time to disease progression of 13 months, and median survival time of 16 months, the company said.

"Based upon data seen in two phase I studies, DCVax-Brain allowed patients not only to live longer but to enjoy more time before disease progression," Liau said. "Glioblastoma multiforme is an aggressive and lethal form of brain cancer. Currently, physicians have little to offer patients with this difficult diagnosis. Broader phase II clinical studies of DCVax-Brain will allow us to build upon the promising data seen in our two phase I studies, and may one day represent a better therapeutic alternative for patients with this deadly tumor type."

The phase II trial will focus on newly diagnosed GBM patients, administering DCVax-Brain early in the course of the disease. The trial will include a regime of booster shots in addition to the initial series of injections.

"FDA clearance of this phase II trial for brain cancer represents the second major clinical milestone achievement this year for Northwest Biotherapeutics, following FDA clearance in January of a large phase III trial for prostate cancer," said Alton Boynton, president and chief operating officer. "We are excited about the data to date, showing substantially greater delays in disease progression and improvements in patient survival than any existing treatments have been able to deliver for patients. We are also pleased to see the lack of any material toxicity in patients receiving our DCVax products."

* * *

OSI Pharmaceuticals Inc. (NASDAQ:OSIP) of Melville, N.Y., and **Genentech Inc**. (NYSE:DNA) of South San Francisco said OSI submitted a supplemental NDA FDA for Tarceva (erlotinib) plus gemcitabine chemotherapy for advanced pancreatic cancer where there has been no treatment.

Tarceva is the first drug to improve survival in a phase III trial when added to gemcitabine chemotherapy in first-line pancreatic cancer compared to gemcitabine alone, the companies said.

The 569-patient multi-center, double-blind, placebo-controlled trial evaluating Tarceva for locally advanced or metastatic pancreatic cancer upon which the filing was based, was randomized so that patients received Tarceva plus gemcitabine or gemcitabine plus placebo, the company said.

The study demonstrated a statistically significant 23.5 percent improvement in overall survival for patients receiving Tarceva plus gemcitabine compared to patients receiving gemcitabine plus placebo, the company said. Twenty-four percent receiving Tarceva plus gemcitabine were alive after one year compared to 17 percent receiving gemcitabine plus placebo. Median survival in the Tarceva plus gemcitabine arm was 6.4 months compared to 5.9 months in the gemcitabine plus placebo arm. An exploratory analysis of survival by pre-treatment characteristics also showed that patients with metastatic disease and patients with poor performance status derived a survival benefit. Progression-free survival in the Tarceva plus gemcitabine arm also was improved, although there was no difference in tumor response (9 percent receiving Tarceva plus gemcitabine versus 8 percent in the gemcitabine plus placebo arm), the company said.

* * *

Reata Pharmaceuticals Inc. of Dallas said RTA 744 has received FDA clearance to begin clinical testing for advanced brain cancers.

The company said it will change its name from Reata Discovery Inc. to Reata Pharmaceuticals Inc. to reflect the clinical status of its drug development programs.

RTA 744 is an anthracycline derivative that crosses the blood-brain barrier for primary and metastatic brain cancers, the company said.

* * *

Sunesis Pharmaceuticals Inc. of South San Francisco said it has obtained worldwide development and commercialization rights to BMS-387032, now SNS-032, a targeted small molecule anti-cancer compound from **Bristol-Myers Squibb Co.** (NYSE: BMY).

SNS-032 is a cyclin dependent kinase inhibitor that induces cell-cycle arrest and apoptosis, the company said.

Under the agreement, BMS would receive an up-front equity stake of $8 million in Sunesis, the company said. Sunesis said it would make a series of additional milestone payments of up to $29 million in cash and equity based on the development and approval for the first indication and formulation of SNS-032.

Additional development and commercialization milestones could total up to $49 million in cash and equity, the company said. In return, Sunesis would receive an exclusive, worldwide license to SNS-032 and future CDK inhibitors derived from related intellectual property.

"In preclinical studies, SNS-032 has demonstrated anti-tumor activity in multiple solid and hematological tumor models," said Daniel Swisher, CEO of Sunesis. "In 2005, we will begin a phase I trial for advanced solid tumors and relapsed lymphoid malignancies."

Clinical Trials:

Adherex Begins Phase II Trial Of Exherin For Eight Tumors

Adherex Technologies Inc. (AMEX:ADH) of Research Triangle Park, N.C., said it has initiated a phase II trial of ADH-1, Exherin, at the Ottawa Regional Cancer Centre in Ottawa, on eight tumor types that express N-Cadherin.

The study would evaluate the anti-tumor activity and tolerability of repeated doses of ADH-1 on an every three-week schedule for tumors the molecular target, the company said. The open-label trial is expected to include up to two additional sites in Canada.

The trial, of up to 60 patients, would include breast and lung as well as adrenocortical and esophageal cancers, the company said.

ADH-1 is a molecularly targeted anti-cancer drug that selectively targets N-cadherin, a protein that holds together and stabilizes cells that make up blood vessels and certain tumor cells, the company said. In the phase I trial, the drug has been well tolerated and has displayed evidence of anti-tumor activity in certain patients.

* * *

Aphton Corp. (NASDAQ:APHT) of Philadelphia said results from its phase II trial of IGN101 for solid tumors demonstrated a statistically significant difference in overall survival in a subgroup of patients with rectal cancer and a positive trend toward survival improvement was observed in colon cancer.

IGN101 was acquired by Aphton through its recent acquisition of Igeneon AG, an Austrian based biopharmaceutical company, the company said.

The randomized, double-blind, placebo-controlled trial was conducted in 240 patients with epithelial cancers, which consists of colorectal cancer, gastrointestinal tract cancer, non-small cell lung cancer and liver cancer, the company said. All patients had metastatic disease (stages III and IV).

The primary objective was to assess the effects of IGN101 on overall survival and an exploratory analysis on subgroups of patients by indication. Secondary endpoints included safety, tolerability and immunogenicity. Vaccinations with IGN101 or placebo were given on days 1, 15, 29 and 57 and in weeks 16, 24, 32, 40 and 68, the company said.

Data came from 239 evaluable patients, of whom 163 had colorectal cancer, 32 had upper GI-tract cancer, 38 had non-small cell lung cancer and 6 had liver or bile-duct carcinoma, the company said. Groups were well balanced regarding age, sex, performance status and concomitant therapies.

For the intent-to-treat population, no difference in overall survival was observed, however, a statistically significant survival prolongation was observed in the 53 stage IV rectal patients.

Median survival in rectal cancer was 415 days for patients receiving IGN101, compared to 253 days for those receiving placebo ($P = 0.037$). Analysis of 1-year survival indicated that survival doubled to 62 percent for patients receiving IGN101 from 29.5 percent for those receiving placebo. A trend for prolonged survival was also observed in stage IV colon during the first year.

Twelve-month survival was 60 percent for patients receiving IGN101 versus 48.8 percent for those receiving placebo ($p = 0.28$). All in the IGN101 group mounted an antibody response to the vaccine antigen. Use of concomitant chemotherapy had no effect on survival. Vaccinations with IGN101 were well tolerated, the company said.

IGN101 induces an immune response against EpCAM positive tumor cells, the company said. The vaccine is an off-the-shelf product consisting of the murine anti-EpCAM monoclonal antibody 17 1-A adsorbed on aluminum hydroxide. EpCAM is a cell surface glycoprotein present in normal epithelial cells and over-expressed in the majority of epithelial cancers.

A randomized, double-blind, placebo-controlled phase II/III trial is being conducted with IGN 101 for advanced non-small cell lung cancer, the company said. In the trial, IGN 101 is being evaluated as a monotherapy.

* * *

ARIAD Pharmaceuticals Inc. (Nasdaq:ARIA) of Cambridge, Mass., said it has begun enrollment in a multi-center phase Ib trial for the oral dosage form of AP23573, an mTOR inhibitor for relapsed and/or refractory cancers.

FDA designated the agent as a Fast-Track product

for sarcomas, the company said.

The non-randomized, dose-escalation study of up to 150 patients, will evaluate the safety, anti-cancer activity, pharmacokinetics, and bioavailability of AP23573 tablets administered in three different oral dosing regimens, the company said. The trial will take place at three to five centers in the U.S.

An intravenous dosage form of the tablets is being studied in multiple phase II and 1b trials for hematologic malignancies and solid tumors, including bone and soft-tissue sarcomas, prostate, breast, ovarian, non-small-cell lung and brain cancers, the company said. To date, the drug has exhibited a favorable safety profile and broad anti-cancer activity, the company said.

"The availability of both dosage forms should provide added flexibility and therapeutic options as we develop AP23573 as a Fast-Track product for sarcoma," said Camille Bedrosian, chief medical officer of ARIAD.

The small-molecule drug, AP23573, inhibits the cell-signaling protein, mTOR, the company said. The agent also blocks the proliferation and migration of vascular smooth muscle cells. AP23573 is in phase I and II trials solid tumors and hematologic cancers.

* * *

GenVec Inc. (Nasdaq:GNVC) of Gaithersburg, Md., said FDA has given permission for the resumption of its phase II trial of TNFerade for rectal cancer.

The clinical hold issues have been satisfactorily addressed for the rectal and esophageal indications and have therefore been removed from the TNFerade IND, the company said. For the esophageal study, the patient accrual is now completed and closed. Follow-up of in the esophageal study is ongoing.

The trial will be conducted in collaboration with the NCI Surgery Branch to evaluate TNFerade in combination with chemoradiation to improve complete response rates, surgical outcomes and survival, the company said.

"Our clinical results to date with TNFerade in a variety of solid tumors, including pancreatic and rectal cancer, have been very encouraging," said Paul Fischer, president and CEO of GenVec.

* * *

Hana Biosciences Inc. (OTCBB:HNAB) of South San Francisco said it has begun a phase I/II study of talotrexin, PT-523, as a single agent for adult relapsed or refractory acute lymphoblastic leukemia.

The phase I portion of the multi-center study will determine the dose, safety, tolerability and pharmacokinetics of talotrexin for refractory leukemia, including both myeloid and lymphoid leukemias. The phase II component will focus on relapsed or refractory ALL to determine the efficacy of talotrexin, as measured by complete response rate.

"There are no drugs specifically approved for adults with relapsed/refractory ALL," said Francis Giles, professor of medicine and chairman, Section of Developmental Therapeutics, at M.D. Anderson Cancer Center, and principal investigator.

Talotrexin also is completing a phase I trial at Dana-Farber Cancer Institute, Massachusetts General Hospital, and Beth Israel-Deaconess hospital for advanced solid tumors, the company said.

In addition, Hana has initiated a multi-center phase I/II study in non-small cell lung cancer, and is planning a trial in cervical cancer with the NCI Gynecologic Oncology Group.

Talotrexin is a non-classical antifolate that is a water-soluble, non-polyglutamatable analogue of aminopterin, the company said.

* * *

Pro-Pharmaceuticals Inc. (Amex: PRW) said it has begun a 40-patient phase II study of Davanat/5-FU for metastatic colon cancer.

In the study, patients with metastatic colorectal cancer, which has spread, despite treatment with approved therapies, will receive the agent in monthly cycles for at least two cycles or until their disease progresses, the company said.

The study will use the same regimen as the final cohort of phase I: 280 mg/m2 of Davanat and 500 mg/m2 of 5-FU, the company said. The study objective is to document the complete and partial response and the rate of stable disease with Davanat/5-FU therapy when administered in monthly cycles where the tumor has failed to respond to, or has progressed despite standard first- and second-line chemotherapy, and to evaluate the safety of the drug in this population.

Davanat is a proprietary polysaccharide in a Carbosome formation that allows the targeted delivery of chemotherapy drugs to protein receptors, the company said.

The trial has been posted to the www.clinicaltrials.gov Web site and is recruiting patients, the company said.

* * *

Ziopharm Inc. of Charlestown, Mass., said it has begun a 40 patient phase I safety and dosing study of ZIO-101, a proprietary small molecule organic arsenic for diverse blood and bone marrow cancers.

The company said it licensed ZIO-101 and related

compounds from M. D. Anderson Cancer Center. Steven Kornblau of M. D. Anderson is the study leader.

Preclinical data on ZIO-101, an organic arsenic, suggests that because of the higher doses could be given and pharmacokinetic differences between organic and inorganic arsenics, the agent may be active in a range of cancers.

"Having discovered the drug, along with Ralph Zingaro, my colleagues and I are very excited about ZIO-101's potential to treat blood and bone marrow cancers," said Srdan Verstovsek of M. D. Anderson.

Safety and dosing will also be tested in a second phase I study in solid tumors that has begun at M. D. Anderson, the company said.

The second 40-patient trial is led by Luis Camacho of M. D. Anderson. "In prior clinical studies, arsenic trioxide has been established as an effective agent to treat acute promyelocytic leukemia, and in combination with other agents as a treatment for multiple myeloma," said Camacho. "Compared to inorganic arsenic, ZIO-101 is a novel organic compound that in preclinical study appears to be safe at much higher doses and could benefit not only patients with hematological malignancies, but also patients with solid tumors. We are excited to be the first cancer center to test this agent in both the hematological and solid tumor setting."

The phase I trials at M. D. Anderson Cancer Center will be followed by a phase I/II trial for advanced myeloma in the second half of 2005, the company said.

A second clinical-stage compound, ZIO-201, is in a phase I safety and dose ranging study at the Karmanos Cancer Center and a second site will soon be added to that trial.

ZIO-201, an isophosphoramide mustard, is a small molecule licensed from DEKK-Tec of New Orleans and is in a phase I study for late-stage cancers at the Karmanos Cancer Center, the company said

Deals & Collaborations:

Stem Cell Initiative To Proceed With $50 Million 3-Year Pledge

(Continued from page 1)

and provost for medical affairs of Cornell University. "One of Weill Cornell's most distinctive resources is our in vitro fertilization laboratory and now, with this farsighted gift, we will be able to develop and maintain stem cells for research and ultimately for translation into clinical medicine."

Harold Varmus, president of MSKCC, said the institute will follow recognized governance procedures. "Given the novel and evolving nature of some types of stem cell research, the governance of the Tri-Institutional Stem Cell Initiative will include the establishment of an oversight board, as recently recommended by the National Academy of Sciences with regard to research involving human embryonic stem cells," Varmus said.

The initiative will focus on the following four areas:

1. Basic and Clinical Stem Cell Research Projects—Emphasis will be on studies that bring stem cell researchers together with colleagues from other fields, including toxicology, neuroscience, cell cycle research, chemistry, and physics, at any of the three institutions. The Tri-Institutional Stem Cell Initiative will also provide a source of private support for research that cannot be funded through government sources, as well as augment grants for stem cell research from NIH and other government agencies, the institutions said.

2. Innovative Collaboration in Stem Cell Biology—In order to build a broad, fully integrated community of stem cell researchers from all three institutions; funds will be earmarked to support collaborative efforts. The funding will promote joint ventures among researchers and the regular exchange of ideas.

3. Graduate and Postdoctoral Training—The Tri-Institutional Stem Cell Initiative will provide fellowship support to outstanding postdoctoral candidates pursuing advanced research related to adult or embryonic stem cells in any of the laboratories of the three institutions and to PhD and Tri-Institutional MD-PhD students engaged in relevant studies.

4. Shared Stem Cell Facilities—These will include laboratories to be utilized by scientists from all three institutions, with activities ranging from the derivation of new stem cell lines to microarray analysis and bioimaging, the institutions said.

* * *

Correlogic Systems Inc. of Bethesda, Md., said it has formed research collaboration with the **Uniformed Services University of the Health Sciences** and the **Henry M. Jackson Foundation for the Advancement of Military Medicine Foundation** to develop a prostate cancer blood test.

Under the agreement, the entities would collaborate on a first study of up to 2,000 men with specified prostate cancer conditions to expand research on the Correlogic protein pattern recognition approach and technology in prostate cancer, the company said.

Research has demonstrated the effectiveness of

the pattern recognition approach and technology in detecting prostate cancer, the company said.

The second study will be for men undergoing radical prostatectomies to determine whether the Correlogic approach and technology can be extended to distinguish between indolent and aggressive prostate cancer, the company said. Distinguishing whether a prostate cancer is aggressive is important in determining the extent or necessity of treatment. At present, there is no effective prospective test for determining the aggressiveness of prostate cancer, the company said.

* * *

GenoLogics Life Sciences Software Inc. of Victoria, B.C., said it has established a strategic partnership with the **Institute for Systems Biology** of Seattle, a developer of open source tools for data collection and analysis as well as scientific instruments and approaches supporting genomics, proteomics, and high-speed cell sorting, to increase the utility of the ISB open source software tools.

GenoLogics said it would enhance the functionality and usability of the open source tools and integrate them into its industry lab management and informatics platform, ProteusLIMS.

"Our recent successes in providing proteomics researchers with an open and integrating lab management and informatics platform will be further increased by integrating and bundling the ISB tools with ProteusLIMS," said James DeGreef, vice president of product management at GenoLogics.

"We are responding to a strong need in proteomics data management and analysis, and the ISB tools will allow ProteusLIMS to provide open spectra visualization, quantification, and statistical validation of protein and peptide search results, among other things," said

* * *

IMPAC Medical Systems Inc. of Mountain View, Calif., and the Coalition of Cancer Cooperative Groups, have entered into an agreement to incorporate the clinical trial database of the coalition into the IMPAC electronic medical record designed for oncology.

"We estimate that as many as 200,000 newly diagnosed cancer patients each year may be clinically eligible to participate in a clinical trial, yet only about 50,000 patients actually participate," said Robert Comis, chairman and president of the Coalition of Cancer Cooperative Groups. "Our goal is to see that every cancer patient is routinely screened for possible matching to a clinical trial."

* * *

LifeSpan BioSciences, of Seattle, **NEC Corp**. and **NEC Soft** of Tokyo have reached milestones in their collaboration to develop a cancer diagnosis support system for pathologists, physicians and patients.

The diagnostic assistant, based on jointly developed, proprietary image capture hardware and computer software, detects cancer cells in pathology specimens and distinguishes them from non-cancerous cells, the companies said. Through the partnership, LifeSpan, NEC, and NEC Soft would provide a system that offers sophisticated image analysis and advanced diagnostic techniques.

Two milestones have been reached in the collaboration, the companies said. The first is the development of an enhanced version of the LifeSpan proprietary automated image capture system, which can automatically capture high quality images from up to 300 pathology slides. The second is completion of improved software to discriminate cancer cells from non-cancer cells based on their morphologic characteristics at high magnification.

* * *

Miikana Therapeutics Inc. of Fremont, Calif., said it has entered into an exclusive worldwide licensing agreement for the Roche compound, MKC-1.

The orally active, anti-cancer agent has demonstrated activity against breast cancer and non-small cell lung cancer in phase II trials, the company said.

Under the agreement, Miikana said it would develop, manufacture, and commercialize the agent.

"MKC-1 has been tested in over 250 patients, with demonstrated anti-tumor activity in advanced, refractory breast and non-small cell lung cancer patients," said S. Gail Eckhardt, co-founder and clinical oncology advisor of Miikana and director of the Developmental Therapeutics Program at the University of Colorado Cancer Center. "Roche has done extensive work on this molecule and we plan to initiate additional phase II trials by the end of 2005."

MKC-1 is a small molecule, cell cycle inhibitor that arrests cellular mitosis by inhibiting an intracellular target shown to be involved in cell division, the company said. In preclinical studies, durable responses have been observed for previously treated NSCLC and metastatic breast cancers.

* * *

Odyssey Thera Inc. of San Ramon, Calif., said it has an expanded agreement with **Pfizer Inc**. to profile compounds across the Odyssey Thera panel of cell-based assays to characterize mechanism of action and pathway activity in human cells.

The patented technology measures pathway activity within living cells and is applied across signaling pathways relevant to drug discovery in therapeutic areas, the company said. The company said it has validated the approach in its known and unknown drug optimization strategy program, which analyzed the mechanism of action of known drugs and known toxicants across signaling nodes in human cells.

The project with Pfizer will focus on 500 compounds from multiple therapeutic areas, the company said.

"By screening compounds across our panel of assays, we can identify and eliminate unanticipated activity much earlier in the drug discovery and development process, before significant resources are invested in pre-clinical and clinical activities,"said John Westwick, chief scientific officer at Odyssey Thera.

* * *

Quintiles Transnational Corp. of Research Triangle Park, N.C., said it has entered into a three-year three-year preferred provider agreement with **Roche** of Basel, Switzerland, for clinical study management services.

The Roche pipeline includes medications for diabetes, hepatitis, anemia, rheumatoid arthritis and cancer in development, the companies said.

Quintiles and Roche have established committees to oversee the development programs conducted under the agreement, the companies said.

* * *

SRI International of Menlo Park, Calif., said its grant from **National Institute of General Medical Sciences** to model complex mammalian signaling networks based on signaling of the epidermal growth factor receptor has been continued.

The grant supports the mathematical modeling of mammalian signaling and other biological networks, using the SRI formal methods tools, the company said.

Promoting the mathematical modeling of biological systems is a primary goal of NIGMS, which would disseminate such tools to biologists to understand the paradigm of systems biology and to design experiments, the company said. Longer term, the tools could validate therapeutic targets and predict the side effects of experimental therapies.

In the first phase of the project, SRI said it demonstrated a computational approach to create, analyze, and test models of complex EGFR signaling networks.

The approach uses the SRI patent-pending Pathway Logic pathway analysis software, based on the Maude computer language, to model biological entities and processes. SRI said it developed some of these tools as part of a Web-based Pathway Logic viewer that allows multiple queries of graphical models of EGFR biochemistry.

In the second phase, SRI said it would increase the utility and predictive capabilities of Pathway Logic by enhancing the ability of researchers to interact with the models. This phase will include development of the Pathway Logic Assistant, an application of the InterOperability Platform, a separately funded research project to enable the formal methods tools written in the Maude language to communicate and interact with each other. With IOP as the infrastructure, researchers would integrate a user interface, a model repository, new visualization tools, and various biological databases into Pathway Logic.

Pathway Logic said it would create models of large-scale signaling networks in defined cell types--computational models of mammalian cells defined in terms of their molecular responses to specific environmental signals, the company said.

Oncology Management:

OTN Becomes Independent Of Bristol-Myers Squibb

One Equity Partners LLC of New York and **Oncology Therapeutics Network** of San Francisco said they have completed the purchase of OTN from Bristol-Myers Squibb (NYSE:BMY).

The transaction will enable OTN, now an independent company, to strengthen its market position in specialty distribution of therapeutics and services to office-based oncologists and to offer technology, information services and solutions to physicians, the companies said.

"As community-based oncologists face dramatic changes in reimbursement, a greater focus on service-based billing, new coding regulations and shifting standards of care, OTN will continue building a broader set of services that this critical segment of the medical community can rely on to deliver the best care possible for cancer patients," said John Amos, president and of OTN.

OEP is a private equity arm of JP Morgan Chase & Co., the companies said.

OTN provides oncology drugs; supportive care products and related supplies to office-based oncology practices in the U.S.