THE CANCER LETTER

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CALGB Chairman Schilsky To Step Down After 15 Years Leading Cooperative Group

By Kirsten Boyd Goldberg

Richard Schilsky, chairman of the Cancer and Leukemia Group B, an NCI-sponsored clinical trials cooperative group, announced his plan to step down in 2010 after serving 15 years in that position.

Schilsky, a professor of medicine and associate dean for clinical research, Biological Sciences Division, University of Chicago Pritzker School of Medicine, became chairman of CALGB in 1995 after serving five years as vice chairman.

CALGB's board of directors changed the organization's constitution in 2005 to allow Schilsky to serve a third consecutive term.

"At this point, it would be best for all concerned if we adhere to the three-term maximum," Schilsky said. "We have accomplished a great deal,

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In the Cancer Centers:

Memorial Sloan-Kettering Brain Tumor Center Receives $10 Million Pledge From Foundation

MEMORIAL SLOAN-KETTERING Brain Tumor Center received a $10 million commitment for preclinical initiatives from **James** and **Marilyn Simons** through the Simons Foundation. The BTC is involved in research of molecular and cellular properties that drive tumor development and growth. Investigators said they would apply that knowledge to therapies that target cancer cells and the abnormal signaling pathways needed to maintain them. Helping to guide the development of the BTC have been three physicians: **Lisa DeAngelis**, chairman, Department of Neurology; **Philip Gutin**, chairman, Department of Neurosurgery; and **Eric Holland**, neurosurgeon and member of the Cancer Biology and Genetics Program and founding director of BTC, said **Harold Varmus**, president pf Memorial Sloan-Kettering. . . . **CITY OF HOPE** received a $5 million gift from **Orly** and **Shmuel Cabilly**, to support the new Cabilly-Riggs Academic Center. The donation will centralize the Graduate School of Biological Sciences, with dedicated space for teaching laboratories, classrooms and administrative offices, as well as a 150-seat auditorium for scientific seminars. The center, now under construction, is named for Cabilly and **Arthur Riggs**, director emeritus of the City of Hope Beckman Research Institute. The center will be housed within the City of Hope Arnold and Mabel Beckman Center for Cancer Immunotherapeutics and Tumor Immunology. . . . **M. D. ANDERSON** Cancer Center was named among the top employers in the Texas Monthly magazine 2008 list of "Best

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but I also feel that change is good for any organization. For one individual to lead an organization for 15 years is a long time. It's important for the group to have someone who can bring in new perspectives and new ideas."

CALGB is seeking nominations for group chairman.

"We would like to be able to field candidates from as broad a pool as possible," Schilsky said. "There is no requirement that candidates come from CALGB institutions. Our goal is to find the best possible candidates."

The Nominating Committee, led by Hyman Muss, professor of medicine at University of Vermont, plans to present a slate of candidates to the board in June. The group will hold an election in November. The new chairman would take office on April 1, 2010, which allows for a 15-month transition.

Typically, the CALGB chairman would be elected in November and take office the following April. Schilsky said he thought a longer transition would be less disruptive to management of this large and complex cooperative group.

"When I took over as group chair in 1995, even having served for five years prior to that as vice chair of group, it still would have been a difficult transition if I hadn't been able to move two senior staff from the prior headquarters office at Dartmouth to Chicago," Schilsky said.

Historically, CALGB's central office has moved to the group chairman's institution.

"My staff has been very loyal, and I have many people who have been with me for as long as I have been group chair," Schilsky said. "I wanted to be sure that, in fairness to them, they would have the opportunity to know in advance who the new chair would be, whether they would have the opportunity to work with that person, whether they would have to consider moving or not.

"It's theoretically possible that the office could remain permanently in Chicago," Schilsky said. "That would require both the agreement of the new chair, and depending on who that person is and where they are located, some arrangements to be made about if they are not able to be the day-to-day on-site manager of the office, who would that be."

"A National Cancer Center Without Walls"

Schilsky will take office in May as president of the American Society of Clinical Oncology for 2008-09. He is a member of the NCI Board of Scientific Advisors, and he served from 1996-2000 on the FDA Oncologic Drugs Advisory Committee. He has served on dozens of committees advising professional societies, cancer centers, hospitals, and NCI.

Serving as a cooperative group chairman "has been a wonderful part of my career," Schilsky said. "CALGB is a terrific organization. I've loved the job of being a group chair. It has been a terrific opportunity, even as it has gotten more and more complicated over the years."

Stepping down will be "bittersweet," Schilsky said. "But after 15 years, it will probably be time for me to think about what else I might want to do in my career. I will be just about 60 years old in 2010. I figure I have one good job left in me. At the moment, I don't know what that might be, but it might be refreshing for me to have the chance to do something different in the later years of my career."

In the past 15 years, five institutions have joined CALGB: Georgetown, Ohio State, Yale, University of Nebraska, and University of Oklahoma. Those have joined the group's "research powerhouses" such as Memorial Sloan-Kettering, Duke, University of North Carolina at Chapel Hill, University of California San Francisco and University of California San Diego, Schilsky said.

Also, the group has expanded its work in laboratory

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science, biospecimen banking, and imaging. "We have always been a very multidisciplinary group," Schilsky said. "We have a strong surgery committee and strong radiation oncology.

"One of the things I've tried to do, having come at this from the position of having been a cancer center director, is view the cooperative group as a national cancer center without walls," said Schilsky, who served as director of the University of Chicago Cancer Research Center for eight years, from 1991 to 1999.

"As a cancer center director, you have the opportunity to build research programs from the faculty in your institution," he said. "As a cooperative group chair, you have a spectacular opportunity to build research programs from faculty at all of the member institutions. We have been fortunate to have many of the really first-rate cancer centers and academic medical centers in the country as members of CALGB.

"A big part of what a cooperative group chair does is to find the talent that's out there in the member institutions, give those people opportunities, put them in leadership positions when the time is right for them, and then support them and let them develop programs," Schilsky said.

"We have a terrific team in CALGB. Every single one of our committee chairs is a national or international star in their area," he said. "The fact that these folks who are very busy and have many other commitments are willing to devote considerable time and energy—without compensation, mind you—to the work of CALGB, is both a testimony to them personally as well as their belief in the strength and value of the whole organization."

Despite the lack of pay for participation in CALGB, the group doesn't have problems recruiting physicians and scientists, Schilsky said. "You have to be a bit of a salesman, of course, because you don't have much to offer in exchange, other than the opportunity to work with great people and have access to lots of patients and lots of specimens," he said.

"We can't pay anybody to do the work they do in CALGB. Nevertheless, people have generally found it a wonderful intellectual atmosphere to work in."

Concerns For Cooperative Group Program

NCI's clinical trials cooperative groups receive a total of about $155 million a year from NCI. Their structure is unique in NIH-supported research in that the networks of investigators are constantly available to test new therapies at multiple institutions. However, the groups have had difficulty mustering Congressional and NIH support for their budgets.

Leading a cooperative group in the current era of flat funding can be a frustrating exercise in trying to address interesting scientific opportunities with fewer resources, Schilsky said.

"The group budgets have been held flat for a number of years," he said. "Our inflation-adjusted budgets are declining. The number of studies being conducted is declining."

Last fall, NCI officials told the group chairmen that the number of new protocols and letters of intent being submitted to the institute for approval has declined, Schilsky said. "If the number of new protocol proposals is dropping, that is not a good sign for the number of new studies that will be available in the system later this year and next year," he said.

The decline is due to a combination of factors, Schilsky said. "The bureaucratic, administrative, and regulatory gridlock in which we are now mired has made it so difficult and so lengthy to get a protocol activated, that it's a turn-off to many young people who used to come into the group and say, 'This is great. I can get my idea and get a protocol running in six months and get a result in a year and half.' Now, it takes a year and half to get a protocol activated, if you're lucky, and by that time your idea is old news. So I think that people are more discouraged than they have been and there is less enthusiasm for submitting new ideas."

Some of the bureaucratic problems are related to funding, Schilsky said. "Because the groups are so terribly under-funded, we really have only two choices: Either we have to do fewer studies, which feeds directly into this problem of disengaging the young people, or we have to find other sources of money to support the studies we do, which means working more closely with the pharmaceutical industry," he said. "As soon as you begin to do that, it introduces whole new levels of complexity.

"We want to be sure that our studies remain independent investigator-initiated studies, so we have a lot of discussion, oftentimes with the drug companies regarding the study design, but that's usually not even the hard part," he said. "The hard part is when you get into issues surrounding budget negotiations, contract negotiations, which can be very protracted and complicated. We are basically involved in business transactions without having a business infrastructure to support us through these transactions.

"The companies have difficulty understanding that the cooperative groups are not another company," Schilsky said. "It takes a lot of effort on the part of

my staff to explain to companies what we are, how we do business, how we can assure that we have control over the quality of a study, how do we bind our sites to complying with group policies. All of that sort of stuff that lawyers tend to get hung up on. That only adds to the time and effort to get these studies going."

Companies are interested in getting new drug registrations or label expansions, which require FDA's involvement. "You have to bring FDA into the picture," Schilsky said. "We then have to engage with the FDA and they have to review the protocol, and we have to be responsive to their comments.

"All of these things have conspired to make the system way more complicated than it used to be," he said. "It used to be, the groups would get a drug from NCI. The NCI would provide support to do the study, and we would do the study, and that was that. The only interaction that had to occur was between the cooperative group and the NCI.

"Now, increasingly, we still have to work with NCI, but now we have to work with a drug company partner, and then we have to work with FDA, and now we have added in the Central IRB."

Breaking Out of Regulatory Gridlock

NCI and the cooperative groups have tried "streamlining" efforts for the past decade, but the regulatory barriers to getting protocols activated quickly continue. A different approach is needed, Schilsky said.

"The enormous challenge, assuming that there is not going to be a windfall of funding for the cooperative groups anytime soon, is to figure out how to break out of the regulatory gridlock," Schilsky said.

"What it's going to take—and it's not clear that this is possible—is for everybody who exercises some control of the process be willing to give up some control," he said. "NCI needs to take an attitude that their job is to facilitate getting studies done, more so than to oversee how the studies are done.

"Similarly, the FDA has to reexamine some of their positions that just create work, but it's not clearly value-added work. They have the same positions with respect to pharma, but pharma has a lot more resources available to comply with what they require. For the groups, where we don't have the resources, we have to try to negotiate our way out of the requirements, or it brings us back to having to work more closely with pharma to get the resources. So we end up in a lot of loops that take a long time to get out of.

"This is the great challenge, to me," Schilsky said. "The science in cancer research these days is breathtaking. The opportunities to bring that science to bear in developing much more effective therapy is extraordinary.

"We are going to have challenges that are complicated by the fact that all of our common diseases are going to become collections of uncommon diseases as we do more and more molecular subtyping," Schilsky said.

"That only is going to make the challenges we face even greater, because instead of treating non-small cell lung cancer, we are going to start having protocols in patients who have EGFR-mutated non-small cell lung cancer, which is only a small percentage of all non-small cell lung cancer patients," he said. "So we are going to take one of the most common malignancies and turn it into one of the least common malignancies. Then we have to figure out how to do clinical trials in that less common tumor type. That's going to require more intergroup studies, more global studies.

"All of these things add complexity to a system which is already in no way systematic."

One More Round of Grant Renewals

Schilsky will be working on the group's grant renewals over the next year. "If I had timed this better, I would have gotten out the door before having to do all the grant renewal," he said. "The good news is that whoever does take over will have clear sailing for a number of years, because all the grants will have been renewed by the time they take office."

The group holds a U10 grant, a CCOP research base grant, and other federal and non-federal grants and contracts.

"My intention is to keep leading CALGB until I walk out the door on March 31, 2010, and in that time to do everything I can to ensure we have a smooth transition," Schilsky said.

The group issued a notice that it is seeking for group chairman nominations of "outstanding clinical oncologists with strong track records in clinical and/or translational cancer research, experience in the design and conduct of cancer clinical trials and significant administrative experience."

Each candidate should submit a curriculum vitae, bibliography, and letter of application summarizing their interests and qualifications by March 15 to Trinidad Ajazi, tajazi@uchicago.edu, CALGB Group Administrator, Cancer and Leukemia Group B, Central Office of the Chairman, 230 W. Monroe, Suite 2050, Chicago, IL 60606-4703.

In Congress:

"Lives At Risk" From Lags In FDA Science, Funding, Report To Agency Concludes

By Paul Goldberg

FDA is out of step with emerging science, understaffed and "not positioned to meet current or emerging regulatory responsibilities," a group of agency advisors said in report made public earlier this week.

A panel brought together by the agency's Science Board spent a year reviewing the state of the agency, producing a document so frightening that Commissioner Andrew von Eschenbach was forced to disagree with its conclusions.

Though von Eschenbach created the Science Board and asked for the review, he wasn't asking for budgetary recommendations, and according to insiders, asked specifically to have these numbers omitted. Nonetheless, the numbers were included in the report—and discussed at a contentious Congressional hearing Jan. 29.

According to the group, Congress needs to commit to a two-year appropriations program to double the agency's funding and increase the number of employees by 50 percent.

FDA's problems are agency-wide and not limited to any center, Gail Cassel, chairman of the group that drafted the report, said at the hearing of the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce. "Since every regulatory decision must be based upon the best available scientific evidence in order to protect the public's health, we concluded that American lives are at risk," said Cassell, vice president for scientific affairs and distinguished research scholar for infectious diseases at Eli Lilly & Co.

The agency's problems include "politicization, attrition of manpower, poor morale, structural and organizational inadequacies, depleted infrastructure and—most importantly—critical gaps in scientific expertise and technology," advisory board member Garret FitzGerald testified at the hearing.

"We must reorganize the structure of science at the FDA," said FitzGerald, director of the University of Pennsylvania Institute for Translational Medicine and Therapeutics. "Amazingly, FDA presently lacks a Chief Scientific Officer. We believe that such a position of leadership is necessary to guide the restructuring of the agency and provide constant advice to the commissioner."

Moreover, Fitzgerald said the agency's scientists should "become re-engaged with the scientific community through attendance at meetings and encouragement to publish on regulatory science and training."

The agency's approach to drug regulation should be changed, too. "The presently segregated approaches to drug review and evaluation before and after approval for marketing should be integrated," FitzGerald said. "Our information about how a drug works and how safely it works is fragmentary at the time of approval. We must exploit enhanced mega-databases of clinical information, accessed in real time by agency scientists to assess drug safety post-approval."

Also, the agency needs to develop a capability to do laboratory science. "The agency scientists may indeed be suspicious of safety signals, but lack freedom, the expertise, and often the site where confirmatory tests might be pursued," said FitzGerald. "We believe that the FDA needs access to a neutral testing ground—a 'Jet Propulsion Lab.'"

Von Eschenbach praised the report, saying that the agency has started implementing it. However, he was unable to endorse the funding recommendations and, under questioning, rejected some of the strongest criticism.

"We have been consistently working to implement many of the things that the report surfaced as important agendas for FDA. And in addition to that, following the report's presentation to the last meeting of the Scientific Advisory Board, I disseminated that report within the agency and asked each of our center directors to directly respond to recommendations in that report and bring forward their operational plans," von Eschenbach said. "This is not going to get fixed with one intervention."

Rep. John Dingell (D-Mich.), chairman of the committee, pressed von Eschenbach on the report's finding that the agency is unable to protect the public.

"Doctor, the Science Board says FDA doesn't have the capacity to ensure safety of food for the nation," said Dingell. "Is it a true statement or not?"

VON ESCHENBACH: "No, sir, I don't believe that's true."

DINGELL: "You will admit the huge decline in the number of inspections made both of domestic producers, manufacturers and processors, and of foreign processors, and that goes across food, drugs and cosmetics. Is that not true?"

VON ESCHENBACH: "Yes sir, I believe we need to increase foreign inspections."

DINGELL: "The finding says this: 'Recommendations of excellent FDA reviews are

seldom followed.' Do you agree with this finding or not?"

VON ESCHENBACH: "Sir, under my opportunity to lead this agency, I have asked for external reviews and I have responded to those external reviews."

DINGELL: "Doctor, is it true or not?'"

VON ESCHENBACH: "I can only speak to my experience, sir… In my experience…"

DINGELL: "So you are telling me that this statement is not true? You are going to get some mail on this, so you better answer this question carefully."

VON ESCHENBACH: "I appreciate the question, Mr. Chairman, but I am attempting to respond to it in the context of my experience at FDA, not that of my predecessors."

DINGELL: "They come forwards, doctor, with another findings: 'FDA cannot fulfill its mission, because its scientific base is eroding and its scientific organizational structure is weak.' Do you agree with that statement or not."

VON ESCHENBACH: "I believe the scientific base needs to be stronger to respond to the emerging challenges that are occurring in the world of science and technology and in the products that we are called upon to regulate. It's not that it's bad, Mr. Chairman, it's just that it is at a level of excellence that needs to continue to improve and continue to expand."

DINGELL: "Regarding your IT system, they've made some very adverse comments on you operations in disaster recovery plan having no continuity in you agency's IT system. Were you surprised by that finding; yes or no?"

VON ESCHENBACH: "No, sir. And we are in the process of addressing that and remedying that.

DINGELL: "Now, doctor, then on page 5, the report notes that FDA has inadequate emergency backup systems in place and recent system failures have resulted in loss of FDA data. Is that true?"

VON ESCHENBACH: "Yes, sir, we are continuously remodeling and improving that."

DINGELL: "It also says that there is no backup of these records, which include valuable clinical trial data. Is that true?"

VON ESCHENBACH: "The records that we've been receiving previously have been primarily in paper form, and we need to transition to electronic…"

DINGELL: "The answer really, to the question I am trying to ask is yes or no. Is there backup or is there not?"

VON ESCHENBACH: "There needs to be better backup."

DINGELL: "Thank you."

As the hearing concluded, Rep. Henry Waxman (D-Calif.) and Sen. Edward Kennedy (D-Mass.) wrote a letter to Comptroller General of the U.S. David Walker requesting an examination of FDA's staffing, information technology, and other needs.

"Although our government always faces financial constraints, we cannot afford to put FDA, which performs tasks vital to the public health, in a situation in which it cannot succeed," said Waxman and Kennedy wrote. "We know that we are not alone in our concern. Public confidence in FDA, and the foods and medical products it regulates, is waning." The letter is available at www.oversight.house.gov.

The Science Board's report is posted at http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_00_index.html.

The testimony and a webcast of the Oversight and Investigations hearing are posted at http://energycommerce.house.gov/cmte_mtgs/110-oi-hrg.012908.FDASelfAssessment.shtml

Professional Societies:

FASEB Urges 6.7% Increase For NIH For Next Fiscal Year

NIH should receive 6.7 percent increase in fiscal 2008, the Federation of American Societies for Experimental Biology suggested in its funding recommendations for science-based agencies.

The president's budget proposal, which will be announced Feb. 4, is expected to include either flat funding or a budget cut for NIH.

FASEB argues that $31.2 billion would be needed by NIH, an increase from the $29.2 billion appropriation for the current fiscal year. However, counting a transfer to the Global AIDS program, the current NIH budget is $28.9 billion.

Overall, the increase amounted to .46 percent from fiscal 2007 to fiscal 2008.

"In the last five years, NIH budget has failed to keep up with inflation, and we are in danger of sacrificing our nation's dominance in biomedical research and biotechnology as well as risking the status of our research institutions as the envy of the world," the report states. "New opportunities for path-breaking research are going unfunded, and there is a real chance that the number of new therapies under development will begin to decrease."

The funding recommendations are posted at http://www.faseb.org.

In the Cancer Centers:

M.D. Anderson Named One Of Best Workplaces In Texas

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Companies to Work For" in Texas. "It is a great honor to be recognized as one of the top institutions in Texas," said **John Mendelsohn**, president of M. D. Anderson. "This distinction is especially important, because it is based on the feedback from M. D. Anderson employees. I intend to use all of what we learned from the survey to build an even better place to work." Organizations from across the state applied for the award and were evaluated in a two-part process. The first section of the process evaluated the M. D. Anderson workplace policies, practices, demographics, and philosophy. The second section focused on the workplace experience, measuring the feedback of 400 randomly selected employees from an online 65-question survey. . . . **E. ANTONIO CHIOCCA**, chairman of neurosurgery at Ohio State University Medical Center, is the recipient of the 2008 Farber Award for his work in brain tumor research. Sponsored by the Farber Foundation, awardees are selected annually by the American Association of Neurological Surgeons and the Congress of Neurological surgeons for dedication and advanced progress in neuro-oncology. Chiocca holds the Dardinger Family Endowed Chair in Oncological Neurosurgery and co-directs the Esther Dardinger Neuro-Oncology Center. . . . . **MEMORIAL UNIVERSITY MEDICAL CENTER** in Savannah, Ga., received a $1.6 million federal appropriation, made possible by **Rep. Jack Kingston**, a a member of the Defense Appropriations Subcommittee. The funding will support research on the link between obesity and cancer conducted by scientists at the Curtis and Elizabeth Anderson Cancer Institute at MUMC and scientists at Walter Reed Army Medical Center. This is the second round of funding for the project, which received a $1.35 million federal appropriation last December. Memorial researchers **John Risinger** and **Jeff Boyd** serve as principal investigators along with **Lt. Col. Larry Maxwell**, of Walter Reed Army Medical Center.

In Brief:

Lymphoma Foundation Names Fisher To Lead Science Board

LYMPHOMA RESEARCH FOUNDATION elected its volunteer Scientific Advisory Board. **Richard Fisher**, director of Hematology/Oncology Division, Department of Medicine, and the Samuel E. Durand Professor of Medicine at University of Rochester Medical Center, will lead Scientific Advisory Board. He is chairman of the Lymphoma Committee of the Southwest Oncology Group. **Bruce Cheson**, head of hematology and director of hematology research at the Lombardi Comprehensive Cancer Center of Georgetown University Hospital, was named chairman-elect. Cheson also is chairman of the Lymphoma Committee of the Cancer and Leukemia Group B. **Andrew Madoff**, CEO of Abel Automatics. Inc., will lead the Board of Directors. Madoff, a lymphoma survivor, is a member of the NASDAQ Technology Advisory Council. . . . **JOSEPHINE BRIGGS** was named director of the National Center for Complementary and Alternative Medicine. "She has been a leader in trans-NIH activities and her in-depth understanding of NIH and translational research will bring new opportunities to the study of CAM," said NIH Director **Elias Zerhouni**. From 1997 to 2006, Briggs was director of the Division of Kidney, Urologic, and Hematologic Diseases National Institute of Diabetes and Digestive and Kidney Diseases. For the last year and a half she has been senior scientific officer at the Howard Hughes Medical Institute. She follows **Ruth Kirschstein**, formerly the acting director of NIH, who was appointed acting director of NCCAM after the death last May of **Stephen Straus**. . . . **BHEESHAM SETHI** was named senior director of development for the National Coalition for Cancer Survivorship. Sethi was vice president of development at the Silicon Valley Community Foundation in Mountain View, Calif., where he managed the analysis, planning, execution and evaluation of fundraising. . . . **CHRIS TAKIMOTO** has joined the South Texas Accelerated Research Therapeutics Scientific Advisory Board. Takimoto was one of the four physician-scientists who in 2007 founded START, a phase I oncology drug development center in the region, and where he has been its director of pharmacology. He will serve on the START board after beginning a new position as director of translational medicine for Johnson & Johnson/Centocor, where he will work with his former mentor and professor, **William Hait**, global head of oncology research and development. "As head of translational medicine at Johnson & Johnson, I will be responsible for working with laboratory-based scientists conducing biomarker research and with clinical research teams conducting studies of some of the most promising anticancer treatments in development," said Takimoto. . . . **NIH SELECTED** five individuals to serve as members of the Advisory Committee to the Director. The new

members, who join 15 members of the council, are **Mary Beckerle**, **Colleen Conway-Welch**, **Walter Isaacson**, **Thomas Kelly**, and **Keith Yamamoto**. Beckerle is executive director of Huntsman Cancer Institute at the University of Utah. Conway-Welch is professor and dean of Vanderbilt University School of Nursing. Isaacson is president and CEO of the Aspen Institute. He has been chairman and CEO of CNN and the managing editor of Time magazine. Kelly is director of Sloan-Kettering Institute, a research arm of Memorial Sloan-Kettering Cancer Center, and professor at Weill Graduate School of Biomedical Sciences, Cornell University. Yamamoto is professor of cellular and molecular pharmacology and executive vice dean of the School of Medicine at the University of California, San Francisco. . . . **CORRECTION**: A headline in last week's issue of The Cancer Letter provided the incorrect acronym for the National Coalition for Cancer Research. **Jerome Yates** will succeed **William Nelson** as president of NCCR.

Funding Opportunities:

Grant Applications Sought For Research In Epigenomics

NIH plans to invest more than $190 million over the next five years to accelerate an emerging field of biomedical research known as epigenomics.

The NIH is making this a priority in its research portfolio, taking it on as an NIH Roadmap initiative. Grant applications are now being accepted for research on epigenome mapping centers, epigenomics data analysis and coordination, technology development in epigenetics, and discovery of novel epigenetic marks in mammalian cells.

"Disease is about more than genetics. It's about how genes are regulated—how and when they work in both health and disease," said NIH Director Elias Zerhouni. "Epigenomics will build upon our new knowledge of the human genome and help us better understand the role of the environment in regulating genes that protect our health or make us more susceptible to disease."

Epigenetics focuses on processes that regulate how and when certain genes are turned on and turned off, while epigenomics pertains to analysis of epigenetic changes across many genes in a cell or entire organism.

The Epigenomics Program is a trans-NIH effort led by several NIH institutes including the National Institute of Environmental Health Sciences, the National Institute on Drug Abuse, the National Institute on Deafness and Other Communication Disorders, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Neurological Disorders and Stroke, and the National Center for Biotechnology Information of the National Library of Medicine. The program is coordinated by the Office of Portfolio Analysis and Strategic Initiatives as part of the NIH Roadmap.

NIH hopes to achieve the following goals with the Epigenomics Program:

—Coordinate and develop a series of reference epigenome maps, analogous to genome maps, which will be publicly available to facilitate research in human health and disease.

—Evaluate epigenetic mechanisms in aging, development, environmental exposure including physical and chemical exposures, behavioral and social environments, and modifiers of stress.

—Develop new technologies for epigenetic analysis of single cells and imaging of epigenetic activity in living organisms.

—Engage the international community to define standard practices and platforms, to develop new laboratory tools such as antibodies.

The overall hypothesis of the NIH Roadmap Epigenomics Program is that the origins of health and susceptibility to disease are, in part, the result of epigenetic regulation of the genetic blueprint. Researchers believe that understanding how and when epigenetic processes control genes during different stages of development and throughout life will lead to more effective ways to prevent and treat disease.

Additional information about the Epigenomics Program is available at http://nihroadmap.nih.gov/epigenomics/.

For more information about funding opportunities, go to: http://www.nihroadmap.nih.gov/hmp/grants.asp.

Program Announcements

PA-08-050: PHS 2008-02 Omnibus Solicitation of the NIH, CDC, and FDA for Small Business Innovation Research Grant Applications. Parent SBIR R43/R44. Application Due Date: April 5; Aug. 5; Dec. 5. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-08-050.html. Inquiries: Michael Weingarten, 301-496-1550; mw498z@nih.gov.

PA-08-051: PHS 2008-02 Omnibus Solicitation of the NIH for Small Business Technology Transfer Grant Applications. Parent STTR R41/R42. Full text: Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-08-051.html.

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Business & Regulatory Report

Oncology Management:

UnitedHealthcare To Base Coverage Of Outpatient Chemo On NCCN Guide

UnitedHealthcare (NYSE: UNH) of Minneapolis said it would base its benefit coverage for chemotherapy drugs used in outpatient settings on the **National Comprehensive Cancer Network** Drugs and Biologics Compendium, effective March 15.

"The new policy provides clinicians, patients and our customers with a respected, independent reference source for use in making chemotherapy coverage decisions," said Lee Newcomer, senior vice president, oncology, UnitedHealthcare. "It is one of several programs launched after UnitedHealthcare established a dedicated oncology team in 2005 to improve the quality of oncology care for our members."

The NCCN guidelines are based on clinical evidence and the consensus of leading academic cancer centers. "NCCN guidelines have become the most widely used in oncology practice," said Bill McGivney, CEO of NCCN. "UnitedHealthcare is the first national health plan to incorporate NCCN guidelines into our chemotherapy-drug benefit."

Clinical Trials:

Semafore, MMRC, Begin Phase I Study Of Small Molecule Targeting PI3 Kinase

Semafore Pharmaceuticals Inc. of Indianapolis and the **Multiple Myeloma Research Consortium** said a phase I study has begun of the Semafore product candidate, SF1126, a targeted PI3 kinase inhibitor.

The single-agent, dose-escalating, multiple-dose 30-patient trial would evaluate the safety and tolerability of the drug in multiple myeloma with at least two failed treatments, the company said. The Winship Cancer Institute of Emory University is the lead study site.

Semafore said it is one of the first recipients of the LEAD grant from the MMRC sister organization, the Multiple Myeloma Research Foundation, which funds biotechnology companies through the early stages of the drug development process for multiple myeloma treatments .

Semafore said it is evaluating SF1126 as a single agent in a multi-center phase I trial in refractory or advanced solid tumors.

SF1126 is a small molecule conjugate containing a pan-PI3K inhibitor that inhibits all PI3K class IA isoforms and other members of the PI3K superfamily, including DNA-PK and mTOR, the company said.

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Allos Begins Phase IIb Study Of PDX Vs. Tarceva In NSCLC

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said it has begun enrollment in a phase IIb randomized, multi-center study comparing PDX (pralatrexate) and Tarceva (erlotinib) in stage IIIB/IV non-small cell lung cancer cigarette smokers who have failed treatment with at least one platinum-based chemotherapy regimen.

The 166-patient study primary endpoint is overall survival, the company said. Secondary endpoints include response rate and progression-free survival, both compared to Tarceva, and the safety and tolerability of PDX. Karen Kelly, deputy director of The University of Kansas Cancer Center, is study chairman.

Randomization will occur to either the PDX arm or the Tarceva arm, the company said. The PDX arm will receive PDX as an intravenous push administered on days 1 and 15 of a 4-week/28 day cycle. The initial dose of PDX will be 230 mg/m2, which, based on defined criteria, may be increased to 270 mg/m2 or reduced in 40 mg/m2 decrements. The Tarceva arm will receive Tarceva 150 mg/day orally daily for the 4-week/28 day cycle. Both arms will receive concurrent vitamin therapy of B12 and folic acid, the company said.

PDX, a small molecule chemotherapeutic agent, inhibits dihydrofolate reductase, or DHFR, a folic acid (folate)-dependent enzyme involved in the building of nucleic acid, the company said.

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Coronado Biosciences Inc. of San Diego said it has begun treatment in a phase I trial of CNO101 (5-imino-13 deoxy-doxorubicin) for advanced cancer.

Treatment is taking place at Holden Comprehensive Cancer Center at the University of Iowa, the company said.

"Available anthacyclines have some degree of cardiotoxicity that limits their use for treating many types of cancers," said Raymond Hohl, Holden Family Chair, associate director of translational research at the cancer center and head of the study. "As a class they are among the most active of chemotherapy drugs and hence, the prospect of a non-cardiotoxic anthracycline is very exciting."

CNDO101 is a fourth generation, 5-imino-13-deoxy-doxorubicin that is rationally designed to eliminate cardiotoxicity without compromising efficacy, the company said.

Infinity Pharmaceuticals Inc. (NASDAQ: INFI) of Cambridge, Mass., and **MedImmune** of Gaithersburg, Md., said they have initiated a phase Ib trial of IPI-504 in combination with Taxotere (docetaxel) for advanced solid tumors at Memorial Sloan-Kettering Cancer Center.

The open-label, dose-escalation study would establish the safety, maximum tolerated dose and optimal schedule of administration for the drug in combination with Taxotere, the company said. Initial treatment would consist of 75 mg/m2 of Taxotere followed by 300 mg/m2 of IPI-504 on day one of each 21-day cycle. Once an MTD is reached, the trial will expand to enroll up to 20 additional patients.

IPI-504 is a small molecule drug candidate that inhibits Hsp90, the company said.

Kosan Biosciences Inc. (NASDAQ: KOSN) of Hayward, Calif., said it has begun a phase II trial of alvespimycin, its second-generation Hsp90 inhibitor, in HER2-positive metastatic breast cancer.

Alvespimycin disrupts the activity of multiple oncogenes and cell signaling pathways in tumor growth, including HER2, the company said.

The trial would evaluate the safety and anticancer activity of the product as a single agent with no prior Herceptin treatment for metastatic disease except in an adjuvant setting, the company said. Antitumor data in advanced HER2-positive cancer demonstrated antitumor activity of alvespimycin in combination with trastuzumab (Herceptin).

The phase II development plan consists of the

single-agent trial of alvespimycin conducted in Eastern Europe with an enrollment of 30 in a two-stage trial design. Those with HER2-positive metastatic disease and no prior trastuzumab treatment except as adjuvant therapy (with the last dose more than 12 months prior to study entry) would be allowed to participate in the trial. The product will be administered intravenously on a one-hour weekly infusion schedule of 80 mg/m2 for three weeks out of four weeks in repeated cycles, the company said.

Kosan said it also is testing the drug delivered orally in a phase I dose escalation trial.

Nektar Therapeutics (NASDAQ: NKTR) of San Carlos, Calif., said it has begun a phase II development program to evaluate NKTR-102 (PEG-irinotecan) for colorectal cancer.

NKTR-102 uses the Nektar small molecule PEGylation technology platform, the company said.

The first study in the program will investigate the drug in combination with cetuximab as a second-line colorectal cancer treatment in irinotecan-naive patients as compared to treatment with standard irinotecan in combination with cetuximab, the company said.

The study is comprised of two sequential stages. The phase IIa study is an open-label, dose-finding trial in multiple solid tumor types that are refractory to standard curative or palliative therapies. The phase IIb trial is an open-label, randomized, double-arm study in second-line metastatic colorectal cancer. Study participants will be randomized to receive either NKTR-102 and cetuximab or standard irinotecan and cetuximab. The primary endpoint is progression-free survival. Secondary endpoints include response rate, response duration, overall survival, standard pharmacokinetics, and incidence of toxicities.

Northwest Biotherapeutics Inc. (BULLETIN BOARD: NWBO) (AIM: NWBT; NWBS) of Bethesda, Md., said it has begun a phase I/II 30-patient trial of DCVax-L for recurrent ovarian cancer at the University of Pennsylvania Center for Research on Early Detection and Cure of Ovarian Cancer and the Abramson Cancer Center.

The trial has two sequential studies, and comprises a combination of multiple treatment modalities, the company said. DCVax-L forms the cornerstone of the treatment regimen, and is complemented by administration of low doses of other approved drugs as well adoptive transfer of DCVax-L primed T cells belonging to the patient.

The principal investigators are George Coukos and Sarah Kim, and the Penn Investigational New Drug sponsor is Carl June, the company said.

DCVax-L, a therapeutic vaccine, is a personalized immunotherapy made from the dendritic cells and the antigens from tumor tissue of the patient.

In the first study, treatment will first consist of standard surgery to reduce the tumor, the company said. Then limited doses will be given of two existing drugs to improve the immune system and modify the tumor vasculature.

Following the preparatory treatments, a series of three immunizations with DCVax-L, each two weeks apart will be administered, while the low doses of two drugs to keep the immune system and the tumor microenvironment in a beneficial condition will continue to be given, the company said.

The second study, which will be a follow-on to the first study but covered by a separate IND filing, will compare two treatment arms continuing further with the drug and DCVax-L regimen, and adding the adoptive transfer of DCVax-L primed, and expanded T cells, the company said.

The Ovarian Cancer Vaccine Initiative, a private philanthropic organization, is funding the NWBT trial at the Hospital of the University of Pennsylvania, the company said.

Pharmion Corp. (NASDAQ: PHRM) of Boulder and **MethylGene Inc.** (TSX: MYG) of Montreal said enrollment has begun in a 75-patient phase II trial, Trial CL002, evaluating MGCD0103, their isotype-selective histone deacetylase inhibitor product candidate, in combination with Vidaza (azacitidine for injection), the Pharmion DNA demethylating agent, for relapsed or refractory Hodgkin lymphoma or non-Hodgkin lymphoma.

Treatment will consist of 75 mg/m2 of Vidaza either intravenously or subcutaneously in combination with an oral dose of MGCD0103 in 28 day cycles, the companies said. Study objectives include overall response rate, progression free survival and duration of response. The trial will include a pharmacokinetic equivalency study.

Anti-tumor activity has been demonstrated in a phase II study of MGCD0103 as a single agent in relapsed or refractory Hodgkin lymphoma, the companies said. GCD0103 is an orally-administered, isotype-selective HDAC inhibitor, the company said.

Also, Pharmion Corp. said it has submitted an MAA with the European Medicines Agency for Vidaza

(azacitidine for injection) for higher-risk MDS, in the European Union.

Vidaza has been designated as an Orphan Medicinal Product in the E.U. for MDS, the company said. The drug also has been designated as an Orphan Medicinal Product in the E.U. for acute myeloid leukemia.

In another development, Pharmion Corp. said the European Medicines Agency has issued a positive opinion to approve Thalidomide Pharmion in combination with melphalan and prednisone for untreated multiple myeloma in age 65 years or older or ineligible for high dose chemotherapy.

Trubion Pharmaceuticals Inc. (NASDAQ: TRBN) of Seattle said **Wyeth Pharmaceuticals** has initiated a phase I/II trial of TRU-015, the Trubion Small Modular ImmunoPharmaceutical drug candidate for non-Hodgkin's lymphoma.

The trial is a nonrandomized, open label, uncontrolled, single-group assignment study, the company said. Trubion said it is co-developing TRU-015 and other CD20-directed therapies with Wyeth Pharmaceuticals, a division of Wyeth (NYSE:WYE).

In the 120-patient trial efficacy will be evaluated according to disease response and progression status per the International Response Criteria for NHL, the company said.

YM BioSciences Inc. (AMEX:YMI) (AMEX: TSX:) (AMEX:YM) (AMEX:AIM:) (AMEX:YMBA) of Mississauga, ON, said it has received a letter from FDA that its phase II Acute Pain Study of AeroLEF has been placed on clinical hold.

Although FDA clearance was announced in June 2007, a re-review of data from the IND submission prompted the hold decision, the company said.

FDA has requested additional safety information on a small group that experienced oxygen desaturation, a class effect of opioids including fentanyl. The company said it would conduct a subgroup analysis.

To date, no patients have been dosed in the U.S. AP5 study and there are no other ongoing clinical trials of AeroLEF.

AeroLEF is an inhaled-delivery composition of free and liposome-encapsulated fentanyl for moderate to severe pain, including cancer pain, the company said. In contrast to fixed-dose approaches to opioid delivery, where a titration period is often required to determine a suitable dose, the product is being developed as a non-invasive delivery system that enables self-titration.

In another development, YM BioSciences said it has completed accrual in the first 50-patient cohort in its phase II trial of nimotuzumab in combination with irinotecan for colorectal cancer.

The safety profile is consistent with data from previous trials, in that there has been no evidence of the severe side effects frequently seen with approved EGFR-targeting antibodies and small molecules, the company said.

This is a single-arm 100-patient trial in two 50-patient cohorts, consecutively, with the first cohort receiving irinotecan and weekly dosing of nimotuzumab and the second cohort receiving irinotecan with nimotuzumab every two weeks, the company said.

Amil Shah, of at the BC Cancer Agency in Vancouver, is principal investigator. Twelve sites across Canada are participating, the company said.

SGX Pharmaceuticals Inc. (NASDAQ: SGXP) of San Diego said it has opened enrollment in two phase I studies, to evaluate the safety, tolerability and pharmacokinetic profile of SGX523, an internally developed, orally-bioavailable, small molecule inhibitor of the cMET receptor tyrosine kinase.

The open-label, dose escalation studies of the agent will be administered in advanced cancer that has either failed standard therapy or that has no existing standard therapy, the company said. The studies would explore two dosing regimens in parallel.

Medarex Inc. (NASDAQ: MEDX) of Princeton said it has filed an investigational new drug application with FDA for MDX-1411 in CD70-expressing malignancies, with the initial study in clear cell renal cell carcinoma.

The open-label, multi-center, dose-escalation, multi-dose 40-patient phase I trial would determine the safety, tolerability and maximum tolerated dose of the drug as well as characterize preliminary efficacy and pharmacokinetics, the company said.

MDX-1411 is a fully human monoclonal antibody that targets the CD70 receptor, a member of the tumor necrosis factor family, the company said.

In another development, Medarex Inc. said it would receive a milestone payment from its licensing partner, **Amgen**, for advancing an antibody into clinical trials.

The antibody was developed using the Medarex UltiMAb technology and is the fifth UltiMAb-derived antibody in clinical development by Amgen, which includes two UltiMAb antibodies in phase II studies, the company said.

Deals & Collaborations:

Cell Therapeutics Completes Zevalin Purchase From Biogen

Cell Therapeutics Inc. of Seattle said it has completed its acquisition of Zevalin (ibritumomab tiuxetan) from **Biogen Idec**, giving CTI sole responsibility for marketing, sales and development of the drug in the U.S.

The drug will continue to be sold outside the U.S. by Bayer Schering under an agreement between Biogen Idec and Bayer Schering, the company said.

When approved in 2002 for relapsed indolent non-Hodgkin's lymphoma, the product was the first radioimmunotherapy approved by FDA, the company said. In 2006, Biogen Idec reported $16.4 million in U.S. Zevalin sales.

CTI said it made an initial t $10 million payment to Biogen Idec in exchange for control of U.S. marketing, sales, and development of the product. Under the acquisition agreement, CTI said it would pay royalties to Biogen Idec based on the net sales of Zevalin until at least December 2015, and has also agreed to pay up to an additional $20 million in milestone payments if the product receives FDA approval for first-line indications in NHL. CTI said it also has agreed to share the cost of clinical trials of the drug with Bayer Schering.

In addition, Jim Fong has joined as vice president of commercial operations, the company said. Fong was senior director of brand marketing at CV Therapeutics Inc.

Alfacell Corp. (NASDAQ: ACEL) of Somerset, N.J., said it has entered into a licensing agreement with **Strativa Pharmaceuticals** to commercialize Onconase (ranpirnase) in the U.S.

Onconase is being evaluated for unresectable malignant mesothelioma in a confirmatory phase IIIb trial, the company said.

Under the agreement, Strativa will have exclusive marketing, sales and distribution rights to the drug for cancer in the U.S. and its territories, the company said. Alfacell said it would retain all rights and obligations for product manufacturing, clinical development and obtaining regulatory approvals, as well as all rights for non-U.S. jurisdictions where Alfacell does not have Onconase partnerships. Joint oversight committees with members from Alfacell and Strativa will manage the alliance.

BioCurex (OTCBB: BOCX) and **Inverness Medical Innovations** (AMEX: IMA) said they have entered into a licensing agreement for the BioCurex RECAF material and technology.

RECAF, the receptor for alpha-fetoprotein, is a wide-spectrum marker present in malignant cancer cells and absent in most normal cells, and is involved in the development of diagnostic tests for prostate, breast, colorectal, lung and other cancers, the company said.

Under the license agreement, IMI would obtain semi-exclusive worldwide rights to commercialize products using the technology. BioCurex will be paid up-front fees, product and development milestones plus royalties on product sales.

Genmab A/S (OMX: GEN) of Copenhagen said its partner **Roche** has initiated a phase II study of R1507 for recurrent or refractory sarcoma.

The R1507 antibody was created by Genmab under its agreement with Roche and initiation of the trial will trigger a milestone payment to Genmab.

In another development, **Genmab A/S** said enrollment has begun in a phase II study of Ofatumumab (HuMax-CD20) in relapsed Diffuse Large B-Cell Lymphoma relapsed following a stem cell transplant.

The 75-patient trial is being conducted under the Genmab collaboration with GlaxoSmithKline, the company said.

Genomic Health Inc. (NASDAQ: GHDX) of Redwood City, Calif., said it has entered into a collaboration with **Pfizer** on a genomic test to estimate the risk of recurrence following surgery for stage I-III renal carcinoma, clear cell type, that has not spread.

As part of the collaboration, the companies said they would apply the same molecular technology and clinical strategy Genomic Health used to develop its Oncotype DX breast cancer test.

Genzyme Corp. (NASDAQ: GENZ) of Cambridge, Mass., said it has entered into a license agreement with **Moffitt Cancer Center** to obtain exclusive worldwide diagnostic testing rights to the discovery of two proteins, RRM1 and ERCC1, in non-small cell lung cancer.

The expression level of the proteins could predict response to therapy, the company said. Gerold Bepler and his team from Moffitt, have shown that the expression levels of RRM1 and ERCC1 correlate with response to platinum drugs and gemcitabine, the company said. Through the license, Genzyme said it would develop and market a diagnostic test to measure the expression levels of the proteins in NSCLC.

In another development, Genzyme said FDA has approved a supplemental indication for Thyrogen (thyrotropin alfa for injection) in combination with radioiodine to ablate, or destroy, the remaining thyroid tissue for removed cancerous thyroids.

Merck KGaA of Geneva said it has entered into a worldwide licensing and collaboration agreement on behalf of its Merck Serono division with **Idera Pharmaceuticals Inc.** (NASDAQ: IDRA) of Cambridge, Mass., to research, develop and commercialize the Idera Toll-like Receptor 9 cancer agonists.

Under the agreement, Idera would exclusively license the therapeutic oncology applications, excluding their use with cancer vaccines, of its TLR9 agonists, IMO-2055 and IMO-2125, the company said. In addition, Merck and Idera have agreed to engage in a research collaboration to identify follow-on TLR9 agonists, which will be derived using the Idera chemistry-based approach and for which Merck will have the exclusive right to use in oncology applications other than cancer vaccines.

Also, Merck said it has agreed to pay an up-front license fee of $40 million to Idera. Also, Idera is eligible to receive milestone payments of up to $381 million on success in clinical development and commercialization, as well as royalties on sales of any products developed and commercialized by Merck based on IMO-2055, IMO-2125 or the follow-on TLR9 agonists.

M. D. Anderson Cancer Center and **AstraZeneca** (NYSE: AZN) said they will collaborate on research of neuropathic pain caused by cancer chemotherapy.

"Our collaboration with AstraZeneca addresses a critical need in cancer care, which is improving the quality of life of cancer patients," said Charles Cleeland, chairman of the Department of Symptom Research at M. D. Anderson.

IDM Pharma Inc. (NASDAQ: IDMI) of Irvine, Calif., said as part of the its decision to evaluate strategic alternatives, **Sanofi-Aventis** has notified the company of its decision to discontinue participation in the development of Uvidem for melanoma, with all rights to the product reverting to IDM.

IDM said it began a restructuring plan to reduce its infrastructure and operating expenses that would be finalized and approved by the board of directors during the first quarter of 2008. The company said it would continue to evaluate the Uvidem clinical program, which completed phase II studies with promising results since it now has full rights to its product candidates including mifamurtide (L-MTP-PE), IDM-2101 and Uvidem.

IDM Pharma said it would work with Sanofi-Aventis to conclude the Uvidem collaboration within the three-month timeframe prescribed in their agreement. As of September 2007, Sanofi-Aventis owned 7.9 percent of the IDM outstanding common stock.

InSightec Ltd. of Tirat Carmel, Israel, said FDA approved an investigational device exemptions application for a phase III study to determine if its ExAblate incisionless surgery system can reduce pain in bone metastases where response to radiation therapy has failed.

The non-invasive, ionized radiation-free magnetic resonance-guided focused ultrasound system was approved for symptomatic uterine fibroids in 2004, the company said.

Using the ExAblate system, MRI is first used to visualize the anatomy and then the system aims focused ultrasound waves at the tumor to thermally ablate, or destroy it, the company said.

The MRI allows the physician to monitor and continuously adjust the treatment in real time, the company said. The patient is consciously sedated to alleviate pain and minimize motion. Due to the high acoustic absorption and low thermal conductivity of the bone cortex, it is possible to use a low level of energy and still achieve a localized heating effect while minimizing damage to adjacent tissue, the company said.

InSightec said it would enroll 148 subjects in the study, which would take place at 15 centers throughout the U.S. and internationally. The company said it is in the process of obtaining Institutional Review Board approval from each of the following sites; including Brigham & Women's Hospital, Fox Chase Cancer Center, Memorial Sloan Kettering Cancer Center, Weill Cornell Medical College, Mount Sinai, Lahey Clinic, the Mayo Clinic, University of California, San Diego Medical Center; and Houston Methodist.

Morphotek Inc., of Exton, Penn., said it has signed a Cooperative Research and Development Agreement with NCI to develop therapeutic antibodies forProCa-1, a cancer-associated protein identified by NCI.

Morphotek said it would apply its proprietary Morphodoma 174 antibody technology to develop therapeutic antibodies for prostate cancer. NCI will evaluate the lead antibodies for therapeutic efficacy.

Oncothyreon Inc. (NASDAQ: ONTY) (TSX:

ONY) of Bellevue, Wash., said it has completed the transfer of assays and methodology related to Stimuvax (BLP25 liposome vaccine) to **Merck KGaA** of Darmstadt, Germany, triggering a payment to Oncothyreon of $5 million.

Merck KGaA said it is conducting a phase III trial of the drug in unresectable stage III NSCLC. The 1300-patient trial, known as Stimulating Targeted Antigenic Responses To NSCLC, or START, would assess survival in treatment with best supportive care and Stimuvax compared to best supportive care alone, the company said.

START is a randomized, double-blind, placebo-controlled study was designed with consideration of scientific advice from the European Medicines Agency and has been agreed upon with FDA through a Special Protocol Assessment.

Rosetta Genomics Ltd. (NASDAQ: ROSG) of Rehovot, Israel, and North Brunswick, N.J., said it has signed a collaboration agreement with the **Henry Ford Health System**, of Detroit to develop microRNA-based diagnostics and prognostics for brain cancer.

Under the collaboration, the parties will conduct a genome-wide molecular analysis of human brain cancer tumors to identify microRNA biomarkers for diagnostic purposes. From the analysis, Rosetta Genomics said it would use its proprietary microRNA extraction technologies to perform a microRNA analysis from Formalin Fixed Paraffin Embedded samples from Henry Ford Hospital.

In another development, **Rosetta Genomics Ltd.** and **Columbia University Medical Center** said they will collaborate on microRNA-based diagnostic tests, early detection as well as prognosis, for diffuse large cell lymphoma, transformed follicular lymphoma, and chronic lymphocytic leukemia.

Vical Inc. (NASDAQ: VICL) of San Diego said it has received a $2.1 million cash payment from **AnGes MG Inc.** for costs associated with the ongoing phase III trial of Allovectin-7 Immunotherapeutic for metastatic melanoma.

AnGes is funding the trial under a collaborative agreement through a scheduled series of cash payments and equity investments totaling $22.6 million, for which AnGes received exclusive marketing rights in Japan and other Asian countries, the company said. AnGes also will receive royalties for sales in the U.S. and Europe. Vical said it is conducting the trial in accordance with a Special Protocol Assessment completed with FDA.

Product Approvals & Applications:

Cephalon Submits NDA For Treanda For B-Cell NHL

Cephalon Inc. (NASDAQ: CEPH) of Frazer, Penn., said it has submitted a New Drug Application to FDA requesting approval of Treanda (bendamustine HCl) for Injection for indolent B-cell non-Hodgkin's lymphoma that has progressed during or following treatment with rituximab or a rituximab-containing regimen.

The NDA is supported by three studies in NHL, including one in combination with rituximab, the company said. In the studies, treatment with Treanda had a high rate of response and a manageable and tolerable side effect profile, with adverse events similar to other chemotherapy agents.

Clinical data on the product, a hybrid of a purine analog and an alkylator, has demonstrated that it acts in two ways to kill cancer cells: it promotes apoptosis and mitotic catastrophe, the company said.

Agennix Inc. of Houston said FDA has reviewed the design of a single phase III trial of its lead molecule, talactoferrin alfa, in combination with chemotherapy in non-small cell lung cancer under the Special Protocol Assessment process.

In randomized, double-blind, placebo-controlled phase II NSCLC trials, talactoferrin or placebo was administered either in combination with chemotherapy in chemo-naive patients, or as monotherapy for those who had failed chemotherapy, the company said. Both trials met primary endpoints--improvement in response rate (first-line combination trial) and improvement in survival (monotherapy trial), with supporting trends on secondary efficacy endpoints. Both trials also showed statistically significant reductions in total adverse events and in significant (grade 3 or higher) adverse events in the talactoferrin arms, the company said.

Separately, Agennix said it received Scientific Advice from the European Medicines Agency indicating that the single phase III trial will also support a Marketing Authorization Application in the European Union.

Agennix said it would initiate phase III trials in both NSCLC indications--talactoferrin in combination with chemotherapy in previously untreated patients and talactoferrin monotherapy where two or more therapies have failed.

The phase III, multinational, randomized, double-blind, placebo-controlled study would enroll 1,100 untreated with stage IIIB or IV NSCLC, the company

said. Randomization will occur for up to six cycles of standard chemotherapy (carboplatin + paclitaxel) plus either oral talactoferrin or placebo. Following six cycles of chemotherapy, or discontinuation prior to six cycles for reasons other than progression, talactoferrin or placebo as maintenance therapy will be administered until disease progression.

Barr Pharmaceuticals Inc. (NYSE: BRL) of Montvale, N.J., said its subsidiary, **Barr Laboratories Inc.** has received final approval from FDA for its generic version of the **Roche Laboratories Inc.** Kytril (granisetron hydrochloride) Tablets, 1mg.

The tablet is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin, and, nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation, the company said.

Celldex Therapeutics of Phillipsburg, N.J., said FDA has granted Fast-Track designation to CDX-110 for EGFRvIII expressing Glioblastoma Multiforme.

CDX-110 is an immunotherapy that targets the tumor-specific growth promoter EGFRvIII that can be expressed by GBM, the company said.

In the ACTIVATE phase IIa study, treatment with the agent showed a median survival time of 30 months, more than a 100 percent increase in survival, versus the historical control median of 14.5 months, the company said. A median time-to-progression of 13 months (p=0.0001) versus the historical control median of 6.4 months was demonstrated. GBM that recurred after treatment with CDX-110 consistently lost EGFRvIII expression with its aggressive growth signal, the company said.

An extension study, ACT II, which combines CDX-110 with chemotherapy in a similar population, has not yet reached median time-to-progression or survival, the company said. Preliminary progression free survival and overall survival data in ACT II look similar to the ACTIVATE experience, and the data suggest that chemotherapy and CDX-110 can be administered concurrently while still maintaining strong immune responses, the company said.

In September, Celldex said it randomized its first patient into ACT III; a definitive phase II/III randomized study of the drug with radiation and temozolomide in newly-diagnosed GBM. The trial is investigating the anticancer activity, impact on survival, and safety of the addition of CDX-110 vaccine to standard of care, versus standard of care alone.

GlaxoSmithKline (NYSE: GSK) said it has received a complete response letter from FDA on its application for Cervarix, a vaccine for cervical cancer.

"We are addressing the questions and will be in discussions with FDA to finalize our responses," said Barbara Howe, vice president and director, North American vaccine development, GlaxoSmithKline.

The application for the vaccine included safety, efficacy and immune response data from trials 30,000 females age 10 to 55 years from ethnically and racially diverse populations, the company said.

Kiadis Pharma of Amsterdam said it has successfully completed an end of a phase II meeting with FDA for Reviroc for elimination of cancer cells from an autologous graft in bone marrow transplantations for end-stage blood cancer.

FDA offered Kiadis Pharma its Special Protocol Assessment procedure allowing Kiadis Pharma to work directly with FDA to optimize the clinical design of the trial, the company said.

The FDA meeting followed the completion of a multi centre phase II study for Reviroc showing an improved overall survival after autologous bone marrow transplantation in Non-Hodgkin's lymphoma, the company said. The phase III trial design for Reviroc will focus on Large B cell lymphoma.

Pharmacyclics Inc. (NASDAQ: PCYC) of Sunnyvale, Calif., said it has received a non-approvable letter from FDA for its NDA of Xcytrin (motexafin gadolinium) Injection for non-small cell lung cancer with brain metastases.

Pharmacyclics said it completed enrollment in three phase II trials evaluating the drug as a single agent, in combination with Taxotere (docetaxel), and in combination with Alimta (pemetrexed).

Oncolytics Biotech Inc. (TSX: ONC, NASDAQ: ONCY) of Calgary, said U.S. NCI has filed a protocol with FDA for a phase I/II trial in metastatic ovarian, peritoneal or fallopian tube cancers using concurrent systemic and intraperitoneal administration of Reolysin, the Oncolytic proprietary formulation of the human reovirus.

NCI is sponsoring the trial under its Clinical Trials Agreement with Oncolytics. The 70-patient trial is taking place at The Ohio State University Comprehensive Cancer Center.