THE CANCER LETTER

Vol. 33 No. 44
Nov. 30, 2007

PO Box 9905 Washington DC 20016 Telephone 202-362-1809

NCI Plans Program To Help Academics With Initial Stages Of Drug Discovery

By Kirsten Boyd Goldberg

NCI officials are designing a program that would assist academic investigators with the initial stages of discovery and development of therapies that modulate molecular targets.

The proposed program, called the Chemical Biology Consortium, would identify findings stemming from NCI R01 grants or other academic research and help investigators take the next step in developing assays to screen for a large number of molecules to find drugs to treat cancer.

The consortium would serve as a link between the discovery that takes place in R01 grants and the drug toxicology, reformulation, and preclinical development that is available in NCI's Rapid Access to Intervention

(Continued to page 2)

In the Cancer Centers:

Young Reappointed Chairman Of NCI's BSA; Curran Moves From Jefferson To Emory

ROBERT YOUNG, chancellor of Fox Chase Cancer Center, was reappointed to a two-year term as chairman of the NCI Board of Scientific Advisors. NCI Director **John Niederhuber** also appointed 10 new board members: **Christine Ambrosone**, of Roswell Park Cancer Institute; **Michael Caligiuri**, director of the Ohio State University Comprehensive Cancer Center; **Curt Civin**, of Johns Hopkins University; **Marc Kastner**, of Massachusetts Institute of Technology; **Timothy Kinsella**, of Case Western Reserve University; **James Omel**, a volunteer with the Leukemia, Lymphoma, and Myeloma Society; **Stuart Schreiber**, of Broad Institute of Harvard and MIT; **Bruce Stillman**, president and CEO of Cold Spring Harbor Laboratory; **Victor Strecher**, of University of Michigan; and **Irving Weissman**, director of Stanford University Comprehensive Cancer Center. . .

WALTER CURRAN was named professor and chairman of the Department of Radiation Oncology at Emory University School of Medicine and chief medical officer of the Winship Cancer Institute, said **Thomas Lawley**, dean of the School of Medicine, and **Brian Leyland-Jones**, WCI director. Curran, a radiation oncologist known for his work in aerodigestive and neurologic malignancies, was professor and chairman of the Department of Radiation Oncology and clinical director for the Kimmel Cancer Center, Jefferson Medical College at Thomas Jefferson University. He is group chairman and principal investigator of the Radiation Therapy Oncology Group, a role he will continue after moving to Emory. "Curran is internationally respected for

(Continued to page 8)

NCI Programs:
Chemical Biology Consortium Needs To Be "Very Unique" To Justify Existence At the Expense Of "Sacred R01s," NCAB's Chabner Says
. . . Page 3

NCI News:
New Model Provides Better Estimate Of Breast Cancer In Black Women
. . . Page 5

FDA News:
Reagan-Udall Board Appointed; Advisory Committee Process Improved, FDA Says
. . . Page 6

Professional Societies:
AACR Plans To Open An Office In Singapore
. . . Page 7

Funding Opportunities:
. . . Page 8

Consortium Would Serve As A Drug Discovery Group

(Continued from page 1)

Development program, NCI Director John Niederhuber said to NCI advisory boards in recent weeks.

With the consortium, NCI would, in effect, "establish a cancer drug discovery group on the scale of a small biotechnology concern" that would "focus on unmet therapeutic needs in oncology not currently addressed by the private sector," Niederhuber said to the National Cancer Advisory Board at its Nov. 27 meeting.

"We have spent a lot of time in the past six months or so developing the Chemical Biology Consortium that is kind of the front end of our drug development platform," Niederhuber said to the NCI Board of Scientific Advisors on Nov. 15. "The long-term vision of the CBC is to bridge the gap between basic scientific investigation and clinical research supported by the NCI as a first step in re-establishing the NCI as a world leader in the area of innovative cancer therapeutics discovery."

NCI officials plan to describe the consortium in greater detail in presentations to NCI advisory boards in the spring, James Doroshow, director of NCI's Division of Cancer Treatment and Diagnosis, said to The Cancer Letter.

It's unclear how much funding NCI would commit to the proposed consortium, Doroshow said. The institute's budget for the current fiscal year is uncertain due to the inability of the administration and Congress to agree on appropriations. "We don't know what our budget is going to be, so whether or not this concept goes forward is budget-permitting," he said.

An Alternative To Licensing

The idea for the consortium arose from talking with academic investigators, Doroshow said in an interview.

"What we have not done for many years outside of the grant pool is to provide resources to help facilitate academic drug discovery," Doroshow said. "If an investigator discovers, in an R01 grant, a completely novel receptor or target that might be involved in a pathway important for cancer, what we have not done for those investigators is to help them with the development of assays that could be used to screen large numbers of molecules."

Over the past three years, the NIH Roadmap has funded centers to develop assays, screen for potential molecules that interrogate assays or might lead to molecules that could be used to develop drugs, and to undertake specialized chemistry to determine how to develop better molecules, Doroshow said. One example is the Scripps Institute, which has a large screening program funded by the Roadmap.

"There have been some dramatic changes in the past five to seven years in the way the chemistry and the screening is done, to optimally define and develop probes and then drugs from probes when one discovers a new target," Doroshow said.

Once an R01 investigator "makes the basic observation and then wants to interrogate further and find molecules that might eventually become drugs, it's hard to find the resources to do that, because either the facilities are too complex or the resources are not organized in academic medical centers to do this," Doroshow said.

"We believe there is this need for us to help facilitate the drug discovery process by providing resources to chemists and biologists who can help work with their own molecules or take molecules in from other academic investigators and help speed the development of not just probes, but eventually drugs that can move along through the pipeline," he said.

Licensing to the industry isn't always the answer in these situations, Doroshow said. Even if an investigator is able to license a molecule to a firm, "often things get licensed, but then get put on a shelf and never tested because there aren't enough resources to take something all the way from the initial lead molecules into the

THE CANCER LETTER

® The Cancer Letter is a registered trademark.

Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
Letters to the Editor may be sent to the above address.

Subscriptions/Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
General Information/FAQ: www.cancerletter.com

Subscription $365 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc.
Founded Dec. 21, 1973, by Jerry D. Boyd.

clinic," Doroshow said.

"We want to provide a pathway for that to happen, especially around areas of biology that are perhaps not the major emphasis of current pharma activity," he said.

For example, NCI wouldn't be interested in EGFR receptors, because "we already have approved drugs in that area and the receptor tyrosine kinases are already the focus of major pharmaceutical investigation," Doroshow said.

On the other hand, "there have not been to date a great deal of effort in the area of trying to find drugs that target transcription factors, because the chemistry is very difficult," he said. "We would be interested in stimulating areas where it may be relatively high risk to go after a particular target, because the commercial payback would be years off."

NCI also would be interested in molecular abnormalities in rare diseases. "We would be interested in facilitating that, and big pharma is not likely to take on such projects," he said.

The proposed consortium "would be the early step of helping to identify molecules around specific biological targets," Doroshow said.

RAID: "The Middle Piece Of Development"

NCI's RAID program spends about $8 million to $10 million a year in direct costs to take a series of projects and "move them through the middle piece of development," Doroshow said.

Established nine years ago, RAID provides resources "to investigators who come to us already with something that is pretty far along the discovery pipeline and we provide access to resources in the development pathway," Doroshow said. "We do a variety of things—maybe a little, maybe a lot—and it can be all the way to getting ready for the drug application and producing the drug to be used in patients."

A review of RAID by a committee led by M.D. Anderson Cancer Center President John Mendelsohn resulted in streamlining the program, Doroshow said. A group of external scientists, half academia and half from industry, advise the program on selecting the concepts to move forward.

In his report to the NCAB, Niederhuber provided an example of a drug that went through the RAID program and is being tested in patients. Fenretinide (4-HPR) was developed at Johnson & Johnson in the 1970s as a chemopreventive, but never looked at as a chemotherapy agent and "sat on the shelf," Niederhuber said. The drug was brought to RAID by C. Patrick Reynolds, of Children's Hospital Los Angeles.

At NCAB, Niederhuber cited an anecdote:

A 26-year-old woman whose cutaneous T-cell lymphoma wasn't responding to other therapies experienced a complete remission in treatment with fenretinide at the NIH Clinical Center. The patient had been bedridden, but after three months of treatment, was able to return home and is without evidence of disease, Niederhuber said.

"This is an example of how NCI's platform is important to the extramural community and to the private sector," Niederhuber said at the meeting.

Altogether, 17 patients were enrolled in a trial, and in addition to one complete response, there were two partial responses, Doroshow said to The Cancer Letter.

"The class of drugs, the retinides, are very interesting, but the problem has been that you could never take enough pills to get enough of these substances in your blood stream," Doroshow said. "What the RAID program did, working with Pat Reynolds, was to develop a novel way to give these almost insoluble molecules intravenously, to get the appropriate amount in the blood stream."

NCAB Concern About Budget, R01s

NCAB member Bruce Chabner, clinical director of the Massachusetts General Hospital Cancer Center, said NCI should play a role in drug development, but the proposed Chemical Biology Consortium would need to be "very unique" to justify the expense.

"In this era, with a constrained budget, I am concerned about how NCI can actually generate enough resources to support a program that has a real impact," Chabner said. "We currently have a biotech industry that is consuming billions of private investment. When our investigators discover a target, usually because they have an R01, they go to industry and form companies and find the capital to do it.

"That process has problems, particularly at the clinical end, where they often don't have a good sense of where they are going and need a lot of help there and NCI can provide it," Chabner said.

"I would love to see this happen, but I think if you are going to have impact on a major scale, it is going to require huge investment, and I'm concerned that we will lose the other side of the issue and that is the investment in basic science, in R01s, as a consequence," Chabner said. "I think it requires a lot of discussion, and I know you have had internal discussions, but where will it be discussed publicly?"

NIEDERHUBER: "Those are certainly concerns, and we have thought a lot about that, and we looked at what we were hearing as the needs. We have been trying to respond more to the needs of the researcher working in academia. That has been the primary driver for response. I will ask Jim Doroshow to respond to this."

DOROSHOW: "We are in the midst of continuing discussions with colleagues in academia both at the discovery end and the clinical end. For some, the connection with biotech has been easier than others. We really see this as a way to help the academic investigators go from beginning to end. Despite the limitations that exist, we have substantial clinical resources, and we have the ability to take things into early therapeutics development. That, happily for us, is still a vigorous activity and reasonably supported. We see this as a way to provide additional resources.

"There have been academic investigators around the country who have told us that the assistance to help them get over the hump, utilizing some resources that have been made available through the NIH Roadmap will allow us to help people get over the hump and get into the clinic with molecules and targets that perhaps are not the primary focus of the industry."

CHABNER: "Maybe we need to hear more about this. My feeling is that it has to be very unique and it has to do something that industry can't do at the present time, and it has to be done on a scale to make a real impact.

"The bottom line is that anything you do here is going to take money away from the sacred R01 pool. This is the font of new ideas, new biology, new targets, and if we cut that off, it's like cutting the head off the animal."

NIEDERHUBER: "We feel we are enabling academia and the private sector. We will do a presentation."

CHABNER: "I think we need to hear about this in detail so we can be convinced there is something really unique and special."

ANTHONY ATALA, an NCAB member and director of the Wake Forest Institute for Regenerative Medicine and chairman of the Department of Urology at Wake Forest University School of Medicine: "I was going to congratulate you on this effort, because in terms of the pharma industry, most of them are shutting down their discovery arms. The pharmaceutical industry is going through major changes.

"One of the problems with the industry is that they change their goals very frequently and shut down programs very quickly. That's one of the challenges we have in discovery. Having a unit to detect these early on is really essential. I think this speaks for the future of this field.

"I think the benefits to patients will be great, like the example you showed. That was an amazing result of the 26-year-old mom of two young children who had this remarkable recovery."

CHABNER: "You can't draw conclusions from one patient. We have so many drugs that one patient has had a response to and the drug has failed totally. That's great, the idea that you have new drugs available is wonderful, and that some patients respond, but you can't draw conclusions from one patient."

ATALA: "You can't. I agree with you there. But in reality, we really do have to change the way we do discovery."

NCAB Chairman Carolyn Runowicz, director of the Neag Comprehensive Cancer Center at University of Connecticut, said the proposal for the consortium would be on the board's agenda for it's spring meeting. She then asked NCAB member Robert Ingram, vice chairman of pharmaceuticals for GlaxoSmithKline, to "give us an insider perspective on industry."

INGRAM: "I can't speak for every company in the industry, but I think, frankly, where we are cutting back is where we need to be cutting back, and that is inefficiencies, particularly in sales and marketing.

"I can speak for GSK, and we want to take our investment in research and development, which today is roughly 18 percent of our revenue, and we want to take that over the next five years to 25 percent. We want to invest more in discovery and development.

"I couldn't agree more with Bruce's comments. Finding the resources that will give John and the whole NIH the ability to do both, to really make this unique opportunity a reality, but also to continue to fund R01 research. I think the industry would really be an ally here, and an advocate to Congress. The companies that will survive and prosper in our industry, whether they are small biotechs—they all want to become big pharma, because that's where the money is—are only going to do so by investing in innovation. What you see happening, say at Pfizer, is restructuring. Yes, you will abandon some programs, but only those programs where you don't think you have an opportunity to make a real difference. Where I think the industry has to get its act together is in the gross inefficiencies in the commercial area. We have way too many sales reps. We can deliver better value to society by taking some of those resources and putting them back into what we are about, and that's the discovery, the development, and ultimately the delivery of medicines."

NCI News:

New Model Better Estimates Breast Cancer Risk In Blacks

A new model for calculating invasive breast cancer risk, called the CARE model, has been found to give better estimates of the number of breast cancers that would develop in African American women 50 to 79 years of age than an earlier model which was based primarily on data from white women.

Both models were designed to be used by health care professionals and should either be used by them or in consultation with them. Researchers at NCI and their collaborators reported on the study methodology and results online in *JNCI* on Nov. 27.

"NCI's Breast Cancer Risk Assessment Tool has been widely used for counseling women and determining eligibility for breast cancer prevention trials," said NCI Director John Niederhuber. "The development of the CARE model highlights the need to develop targeted tools to assess an individual woman's risk, and those tools must be based on many factors that also assure that the tool can be used in a non-discriminatory manner."

The NCI investigators worked with the Women's Contraceptive and Reproductive Experiences (CARE) Study, the Women's Health Initiative, and the Study of Tamoxifen and Raloxifene trial to produce and test the new model. Some members of the team had worked on both the CARE and earlier model, called BCRAT (Breast Cancer Risk Assessment Tool). Because of the higher accuracy of the CARE model for African American women, the NCI authors are now recommending its use for counseling these women regarding their risk of breast cancer.

While the BCRAT allows for projections for African American women and for women from other racial and ethnic groups, these projections are based on certain assumptions. In particular, it is assumed that the relative risk of breast cancer associated with having a specific profile of risk factors for white women applies to African American women and to women from other racial and ethnic groups as well. Because of the need to rely on these various assumptions, rather than on sufficient data from African American women and women in other racial and ethnic groups, BCRAT, which can be found on the NCI Web site at http://www.cancer.gov/bcrisktool, includes a disclaimer for African American women and for women in other groups that their projections might be inaccurate.

To develop a new model that would more accurately assess an African American woman's chance of developing breast cancer, researchers in the CARE study examined data from 1,607 African American women with invasive breast cancer and 1,637 African American women of similar ages who did not have breast cancer. The factors used in the model were age at first menstrual period, number of first degree relatives who had breast cancer, and number of previous benign breast biopsy examinations. A woman's age at the birth of her first child, a risk factor for white women, did not improve prediction in African American women and so was not included in the model. Risk was calculated by combining information on these factors with African American rates of new invasive breast cancer from NCI's Surveillance, Epidemiology and End Results Program and with national mortality data.

To test the accuracy of the model, researchers compared data in the CARE model with data from the 14,059 African American women aged 50 to 79 in the Women's Health Initiative study who had no prior history of breast cancer. From the risk factor profiles for breast cancer that were collected at entry into the WHI, the researchers used the CARE model to estimate the number of women who would be expected to develop invasive breast cancer and found that the model predicted that 323 would be affected, close to the 350 breast cancers in African American women that actually occurred during the WHI follow up.

"The CARE model predicted the numbers of breast cancer diagnoses well overall, and in most categories," said Mitchell Gail, the lead author of this study and an NCI investigator.

One of the key uses of the BCRAT has been to determine eligibility criteria for a number of breast cancer prevention trials. For African American women 45 and older, the CARE model risk projections were usually higher than those from the BCRAT. To assess what the impact of using the CARE model might have been on a recently completed prevention trial, the researchers used eligibility screening data from 20,278 African American women who were examined in the Study of Tamoxifen and Raloxifene (STAR) trial between 1999 and 2004.

The investigators estimated that 30.3 percent of African American women would have had significant five-year invasive breast cancer risks based on the CARE model, compared to only 14.5 percent based on BCRAT.

"African American women were both more interested in and more likely to enroll in the STAR trial compared to the earlier Breast Cancer Prevention Trial, but the recruitment process and our enrollment task

would have been easier if the CARE model had been available," said Worta McCaskill-Stevens, of NCI and one of the leaders of the STAR trial.

Also, inaccurate projections using the BCRAT could result in African American women receiving an underestimate of their breast cancer risk. As a result of this underestimate, African American women might not get counseling about actions they could take to reduce their risk. "There has been great interest in developing race- or ethnicity-specific adaptations of the BCRAT model that are based on sufficient race- or ethnicity-specific data, and the CARE data enabled us to develop the new model," said Gail.

The CARE model, like the BCRAT, needs to be approached with caution or avoided for certain special populations, the researchers said. These models should not be used for women with a previous history of breast cancer. The models tend to underestimate risk in women who have received radiation to the chest and in women who are known to carry mutations associated with increased risk of breast cancer, such as mutations in the BRCA1 and BRCA2 genes. While the CARE model has not yet been incorporated into the BCRAT on the NCI Web site, NCI plans to have the tool updated by the spring of 2008.

FDA News:

Reagan-Udall Foundation Board Members Named

FDA announced the board members of the Reagan-Udall Foundation, a private nonprofit organization created by Congress last September in the passage of the Food and Drug Administration Amendments Act.

Mark McClellan, director of the Engleberg Center for Health Care Reform at the Brookings Institution, former commissioner of FDA and former administrator of the Centers for Medicare and Medicaid Services, will serve as chairman of the foundation.

"The foundation is an unprecedented opportunity to enlist broad-based support to accelerate scientific progress to help FDA fulfill its mission of protecting and promoting the public health—a mission that is more challenging but more important than ever," McClellan said. "I look forward to a collaborative partnership with the board, the agency, legislators, and stakeholders to accelerate innovation that will improve the quality and safety of medical and food products."

Congress established the foundation to identify unmet scientific needs in the development, manufacture and evaluation of the safety and effectiveness of FDA-regulated products, including post-market evaluation.

The board members are: Georges Benjamin, executive director, American Public Health Association; William Brody, president, Johns Hopkins University; Helen Darling, president, National Business Group on Health; Cal Dooley, president and CEO, Grocery Manufacturers Association; Michael Doyle, Regents Professor and director, Center for Food Safety, University of Georgia; Joseph Hogan, president and CEO, GE Healthcare; Kay Holcombe, senior health policy advisor, Genzyme Corp.; Sharon Levine, associate executive medical director, The Permanente Medical Group; Gary Neil, group president, Johnson & Johnson Pharmaceutical Research & Development; Phillip Sharp, Institute Professor, Center for Cancer Research, Massachusetts Institute of Technology; Ellen Sigal, chair and founder, Friends of Cancer Research; Tadataka Yamada, president, Global Health Program, Bill & Melinda Gates Foundation; and Diana Zuckerman, president, National Research Center for Women and Families.

The statute calls for a 14-member board: four representatives from the general pharmaceutical, device, food, cosmetic, and biotechnology industries; three from academic research organizations; two from patient or consumer advocacy groups; one representing health care providers; and four at-large representatives with expertise or experience relevant to the foundation's purpose.

A majority of the foundation's board members—nine out of 14—must be appointed from a list of candidates provided by the National Academy of Sciences and the remaining five from nominations submitted by patient and consumer advocacy groups, professional scientific and medical societies and industry trade organizations.

The FDA commissioner and NIH director will participate as non-voting board members.

FDA Takes Steps To Improve Advisory Committee Process

FDA is announcing several steps to strengthen its advisory committee processes in ways consistent with recommendations of the Institute of Medicine.

The measures include proposed new guidance or procedures on advisory committee voting, on disclosing information on conflicts of interest, and on security and appropriate conduct for participants at meetings. Other improvements include greater clarity to FDA's advisory committee Web site, which can be found at http://www.fda.gov/oc/advisory/default.htm.

"One of FDA's strengths is that we routinely enlist the nation's leading experts to give us public advice on complex medical and scientific issues," said Randall Lutter, Ph.D., deputy commissioner for policy. "The new steps we're taking further enhance the transparency and reliability of our advisory committee processes."

A draft guidance document recommends advisory committees adhere to a process of simultaneous voting, in which all members vote at once. The results of the vote would be announced immediately. How each member voted would be part of the public record. The draft guidance document is available at http://www.fda.gov/oc/advisory/votingguidance.html.

A second draft guidance issued recently lays out recommended changes to the process of public disclosure of financial interests that create conflicts of interest for advisory committee members. The new draft guidance makes the process more transparent and consistent by having all advisory committee members publicly disclose interests for which a waiver is granted. The draft guidance also includes redesigned disclosure and waiver templates that are clearer and easier for the general public to understand. The draft guidance document and redesigned templates are available at http://www.fda.gov/oc/advisory/waiver/ACdisclosure1007.html.

FDA also has formalized operating procedures designed to ensure appropriate security and promote proper decorum and public conduct at advisory committee meetings. They are intended to help ensure that meetings proceed in an orderly fashion and that the work of the committees is not impeded, but that the right of free speech is also protected.

Also, FDA has improved its Web page on advisory committees by providing better access to information about waivers granted for conflicts of interest. The Web site is at http://www.fda.gov/oc/advisory/default.htm.

FDA recently posted the names of outside experts that it has named to a new risk communication advisory committee to make recommendations to FDA about how best to communicate the risks and benefits of FDA regulated products. Further information is available at http://www.fda.gov/bbs/topics/NEWS/2007/NEW01739.html.

The agency asked a consultant, Eastern Research Group, to study 16 recent advisory committees. The report highlights the difficulty of assembling highly qualified experts who are free of conflicts and finds that those who have received waivers appear to be significantly more qualified than those who have not received waivers. The full report is available online at http://www.fda.gov/oc/advisory/ERGCOIreport.pdf.

Professional Societies:

AACR Plans "AACR Asia," An Office In Singapore

American Association for Cancer Research said it plans to establish AACR Asia, an office that will open in Singapore in 2009.

Recent trends have made the Asian Pan-Pacific region an attractive place to engage in cancer science, the society said. Top researchers from around the world are being drawn to Singapore, in particular, because of the country's support for bioscience research and technology.

AACR said the goals of AACR Asia are to: Become a global hub for cancer research information, networking and collaborations; increase cancer research collaborations between the East and West; provide educational opportunities for young scientists in the Asian Pan-Pacific region; boost AACR's insight into cancer and cancer research in the Asian Pan-Pacific region and thus serve as an expert resource in the region; facilitate and influence cancer public health and cancer research policy in the region; further develop collaborations with regional governments, universities, and international non-governmental organizations; identify new development and funding opportunities for cancer research.

Also, the Ludwig Institute for Cancer Research announced an initiative that will focus on translational and clinical cancer research and involve three Singapore institutions: the Agency for Science, Technology and Research (A*STAR), National University of Singapore's Yong Loo Lin School of Medicine, and the Duke-NUS Graduate Medical School.

"The decisions of AACR and Ludwig to locate here will bring to Singapore and Asia valuable resources and networking opportunities that complement the strengths of local healthcare and research institutions," Singapore's Minister for Health Khaw Boon Wan said in a statement.

* * *

AMERICAN SOCIETY of HEMATOLOGY elected three officers to its Executive Committee. **Hal Broxmeyer** will serve a one-year term as vice president, followed by terms as president-elect and president. He is scientific director of the Walther Oncology Center at the Indiana University School of Medicine. Councilors **Thomas Bensinger**, a private practitioner in Greenbelt, Md., and **Stephanie Lee**, associate member of the Fred Hutchinson Cancer Research Center, will serve four-year terms.

In the Cancer Centers:

Arizona Wins $12 Million GI SPORE Grant Renewal

(Continued from page 1)

his work in radiation oncology and in clinical trials," said Leyland-Jones. "Winship's capacity in translational cancer medicine and clinical trials provides a perfect complement to Dr. Curran's chairmanship of RTOG."

. . . **ARIZONA CANCER CENTER** Gastrointestinal Cancer Program received a $12 million Specialized Program of Research Excellence grant from NCI. The five-year grant is a renewal of the first GI SPORE funded in 2002. **Eugene Gerner**, director of the GI Cancer Program, is principal investigator. The renewal includes four major research projects, three cores, and career development and developmental research programs. The SPORE brings together researchers from University of Arizona, including the Health Sciences Center, and the BIO5 Institute. Other collaborators are from M.D. Anderson Cancer Center, University of California Irvine Chao Family Cancer Center, Virginia G. Piper Cancer Center, and the Translational Genomics Research Institute. A supplemental grant to study biomarkers for Barrett's esophagus involves researchers from the University of Arizona, Southern Arizona VA Medical Center, Johns Hopkins, Mayo Rochester, Mayo Jacksonville, University of North Carolina, Vanderbilt, and University of Maryland. A second supplemental study to continue research on the relationship between arsenic exposure and cancer involves a team of investigators from the University of Arizona, Universidad de Sonora, and Instituto Technologico de Sonora.

Funding Opportunities:

RFA-RM-08-004: New Methodologies for Natural Products Chemistry. R01. Letters of Intent Receipt Date: Dec. 23. Application Submission/Receipt Date: Jan. 23. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-RM-08-004.html. Inquiries: John M. Schwab, 301-594-3827; schwabj@nigms.nih.gov.

RFA-CA-08-501: Limited Competition: AIDS and Cancer Specimen Resource. U01. Application Receipt Date: Jan. 15. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-08-501.html. Inquiries: Rebecca Huppi, 301-402-3920; liddellr@exchange.nih.gov.

RFA-RM-07-011: Technology Development in Epigenetics. R01. Letters of Intent Receipt Date: Jan. 14. Application Submission/Receipt Date: Feb. 14. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-011.html. Inquiries: John Satterlee, 301-443-1887; satterleej@nida.nih.gov.

RFA-RM-07-012: Technology Development in Epigenetics. R21. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-012.html.

RFA-RM-07-013: Reference Epigenome Mapping Centers. U01. Letters of Intent Receipt Date: Feb. 7. Application Receipt Date: March 7. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-013.html. Inquiries: Frederick Tyson, 919-541-0176; tyson2@niehs.nih.gov.

RFA-RM-07-014: Epigenomics Data Analysis and Coordination Center – EDACC. U01. Letters of Intent Receipt Date: Feb. 7. Application Receipt Date: March 7. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-014.html. Inquiries: Joni Rutter, 301-435-0298; rutterj@mail.nih.gov.

RFA-RM-07-015: Discovery of Novel Epigenetic Marks in Mammalian Cells. R01. Letters of Intent Receipt Date: Jan. 14. Application Submission/Receipt Date: Feb. 14. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-015.html. Inquiries: Philip Smith, 301-594-8816; smithp@mail.nih.gov.

RFA-RM-07-016: Discovery of Novel Epigenetic Marks in Mammalian Cells. R21. http://www.grants.nih.gov/grants/guide/rfa-files/RFA-RM-07-016.html.

PAR-08-025: Quick-Trials for Novel Cancer Therapies and Prevention: Exploratory Grants. R21. Application Submission/Receipt Date: March 7; July 9; Nov. 7; March 9, 2009; July 9; Nov. 9; March 9, 2010; July 9; Nov. 9. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PAR-08-025.html. Inquiries: Heng Xie, 301-496-8866; xiehe@mail.nih.gov.

PAR-08-026: Support of Competitive Research Research Advancement Award. SC1. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PAR-08-026.html. Inquiries: Hinda Zlotnik, 301-594-3900; zlotnikh@nigms.nih.gov.

PAR-08-027: Support of Competitive Research Pilot Project Award. SC2. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PAR-08-027.html.

RFP 1406-04-08-RP-20201: Data Capture And Management System For Cancer Clinical Research. Response Due date: Nov. 29. Full text: http://www.fbodaily.com/archive/2007/11-November/01-Nov-2007/FBO-01443245.htm. Inquiries: Louis Gilden 703-964-3680; louis.gilden@aqd.nbc.gov.

RFP N02-CM-81000-48: Drug Development Support For The Cancer Therapy Evaluation Program. Response Due date: Dec. 19. Full text: http://www.fbodaily.com/archive/2007/11-November/04-Nov-2007/FBO-01445580.htm. Inquiries: John Manouelian, 301-435-3813, jm486p@nih.gov or Richard Hartmann, 301-496-8620; rh75f@nih.gov.

RFP VA-263-08-RP-0040: Tumor Registry Services. Response Due date: Dec. 7. Full text: http://www.fbodaily.com/archive/2007/11-November/18-Nov-2007/FBO-01453826. Inquiries: Joann Walker joann.walker@va.gov.

Distribution Policy for The Cancer Letter

Thank you for your purchase of this issue of The Cancer Letter! Because issue and subscription sales are our major source of revenue, we wouldn't be able to provide you with the information contained in this newsletter without your support. If you have any questions or comments about the articles, please contact the editors (see page 2 of your issue for contact information).

We welcome your use of the newsletter and encourage you to send articles once in a while to colleagues. But please don't engage in routine distribution of The Cancer Letter to the same people week after week, unless your organization has purchased a site license or group subscription. If you aren't sure, ask the person who is paying for this subscription. If you are sending the newsletter to an unauthorized list, please stop; your actions are against Federal law. If you received this newsletter under an unauthorized arrangement, know that you are in receipt of stolen goods. Please do the right thing and purchase your own subscription.

If you would like to report illegal distribution within your company or institution, please collect specific evidence from emails or photocopies and contact us. Your identity will be protected. Our goal would be to seek a fair arrangement with your organization to prevent future illegal distribution.

Please review the following guidelines on distribution of the material in The Cancer Letter to remain in compliance with the U.S. Copyright Act:

What you can do:

- Route a print subscription of the newsletter (original only) or one printout of the PDF version around the office.
- Copy, on an occasional basis, a single article and send it to a colleague.
- Consider purchasing multiple subscriptions. We offer group rates on email subscriptions for two to 20 people.
- For institution-wide distribution or for groups larger than 20, consider purchasing a site license. Contact your librarian or information specialist who can work with us to establish a site license agreement.

What you can't do without prior permission from us:

- Routinely copy and distribute the entire newsletter or even a few pages.
- Republish or repackage the contents of the newsletter in any form.

If you have any questions regarding distribution, please contact us. We welcome the opportunity to speak with you regarding your information needs.

The Cancer Letter
PO Box 9905
Washington DC 20016
Tel: 202-362-1809
www.cancerletter.com

THE CANCER LETTER

Vol. 22 No. 10
November 2007

Business & Regulatory Report

Product Approvals & Applications:

FDA Approves sNDA For Nexavar In Unresectable Hepatocellular Carcinoma

Bayer HealthCare AG of Leverkusen, Germany, and **Onyx Pharmaceuticals Inc.** (NASDAQ: ONXX) of Emeryville, Calif. said FDA has approved a supplemental New Drug Application for Nexavar (sorafenib) tablets for unresectable hepatocellular carcinoma.

Last month, the European Commission approved the drug for the same indication.

Nexavar, an oral drug, is the first approved systemic drug therapy for liver cancer and the only drug shown to improve overall survival in

(Continued to page 2)

Clinical Trials:

Randomized Phase IIb Trial Tests Nexavar Plus Paclitaxel In Metastatic Breast Cancer

Northwestern University Feinberg School of Medicine McGaw Medical Center said it is collaborating with **Accelerated Community Oncology Research Network**, a contract research organization, on a double-blind, placebo-controlled randomized phase IIb study to evaluate the combination of Nexavar and paclitaxel in recurrent or metastatic breast cancer.

The study will measure how well participants tolerate the study drug, and how quality of life is affected, the institution said. Nexavar is being co-developed by Bayer HealthCare Pharmaceuticals and Onyx Pharmaceuticals is approved for kidney cancer, the institution said.

"To further characterize the activity of sorafenib, the trial will randomize for treatment of weekly paclitaxel or the combination of paclitaxel and sorafenib," said William Gradishar, professor of medicine at the Feinberg School of Medicine of Northwestern University and principle investigator. "The trial will determine if an oral multi-kinase inhibitor adds to the clinical benefit derived from chemotherapy alone in metastatic breast cancer."

The ACORN Contract Research Organization enrolls research sites, provides contract and budgeting services, promotes the accrual of subjects at the site level, collects data and monitors its accuracy, and works as an extension of both the sponsoring organization and the participating research sites, the institution said.

Allos Therapeutics Inc. (NASDAQ: ALTH) of Westminster, Colo., said it has begun a phase I, open-label, multi-center study of its targeted

(Continued to page 4)

Drug Approvals:
EU Approves Torisel
For Renal Cell Cancer
. . . Page 2

Clinical Trials:
Cleveland Clinic Tests
New Chest X-Ray
For Lung Cancer
. . . Page 4

Deals & Collaborations:
Beckman Coulter
To Buy Dako's
Flow Cytometry Unit
. . . Page 6

Oncology Management:
CyberKnife Treats
4,000th Lung Cancer
Patient, Firm Says
. . . Page 7

PO Box 9905
Washington DC 20016
Telephone 202-362-1809

Nexavar Approval For HCC Based On Phase III Trial Data

(Continued from page 1)

the disease, the companies said. In Europe, the agent was approved for HCC in October. In 2005, Nexavar became the first new treatment in more than a decade for advanced kidney cancer and is approved in more than 60 countries for this indication.

The approval was based on the international, phase III, placebo-controlled Sorafenib HCC Assessment Randomized Protocol trial that demonstrated that Nexavar improved overall survival by 44 percent in HCC (HR=0.69; p=0.0006) vs. placebo, the companies said. Median overall survival was 10.7 months with Nexavar treatment compared to 7.9 months to placebo. No indication of imbalances was observed in serious adverse event rates between the drug and placebo-treated groups with the most commonly observed adverse events Nexavar being diarrhea and hand-foot skin reaction.

Nexavar targets both the tumor cell and tumor vasculature, the companies said. In preclinical studies, the agent has been shown to target kinases including Raf kinase, VEGFR-1, VEGFR-2, VEGFR-3, PDGFR-B, KIT, FLT-3 and RET.

In December 2005, the FDA approved Nexavar for the treatment of patients with advanced kidney cancer. In Europe, the drug was approved in July 2006 for the treatment of patients with advanced renal cell carcinoma who have failed prior interferon-alpha or interleukin-2 based therapy or are considered unsuitable for such therapy.

The drug is co-developed by Bayer and Onyx.

Wyeth Pharmaceuticals, of Collegeville, Penn., a division of Wyeth (NYSE: WYE), said the European Commission has approved Torisel (temsirolimus) for the first-line treatment of advanced renal cell carcinoma in patients who have at least three of six prognostic risk factors.

Torisel is the only approved cancer therapy that specifically inhibits the mTOR (mammalian target of rapamycin) kinase, an important regulator of cell proliferation, cell growth and cell survival. The drug was approved in the U.S. last May for the treatment of advanced RCC.

"Temsirolimus was studied in the most difficult-to-treat patients with advanced renal cell carcinoma: those who have multiple risk factors that have been associated with shortened survival," said Bernard Escudier, head of the Immunotherapy Unit, Department of Medical Oncology, Institut Gustave Roussy, Villejuif, France, and an investigator in the Torisel phase III study. "The ability of temsirolimus to provide an increase in overall survival in these patients provides us with a much-needed new option for the treatment of advanced kidney cancer."

Torisel was studied in a three-arm, phase III clinical trial of 626 patients with advanced RCC and three or more of six preselected prognostic risk factors who had received no prior systemic therapy.

In the study, Torisel significantly increased median overall survival by 49 percent compared with interferon-alpha (10.9 months vs. 7.3 months, p=0.0078). Torisel also was associated with a statistically significant improvement over interferon-alpha in the secondary endpoint of progression-free survival (when the disease does not worsen; 5.6 months vs. 3.2 months, p=0.0042). The combination of Torisel and interferon-alpha did not result in a significant increase in overall survival when compared with interferon-alpha alone, the company said.

Bristol-Myers Squibb Co. (NYSE: BMY) of Princeton, N.J., said FDA has approved new labeling for Sprycel to include a lower recommended starting dose of 100 mg once daily and safety and efficacy data in chronic-phase chronic myeloid leukemia resistant or intolerant to prior therapy including Gleevec.

The product labeling also includes data from

THE CANCER LETTER

To subscribe, visit www.cancerletter.com

Business & Regulatory Report
Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724

Business & Regulatory Report is a supplement to The Cancer Letter and available separately for $175 per year. ISSN 1053-9611.

the first randomized trial of Sprycel and Gleevec, the company said. Sprycel is indicated for adults with chronic, accelerated, or myeloid or lymphoid blast-phase CML with resistance or intolerance to prior therapy including Gleevec. The effectiveness of Sprycel is based on hematologic and cytogenetic response rates. There are no controlled trials demonstrating a clinical benefit, such as improvement in disease-related symptoms or increased survival, the company said.

The updated labeling was granted priority review and was approved in six months based on two studies for chronic-phase CML with resistance or intolerance to Gleevec, the company said,

Sprycel is an oral inhibitor of multiple tyrosine kinases.

Roche of Basel, Switzerland, said the European Committee for Medicinal Products for Human Use has issued a positive recommendation for Avastin (bevacizumab) for first-line treatment of renal cell carcinoma.

The decision is based on data from the phase III AVOREN trial, which showed that adding Avastin to interferon doubled life expectancy in advanced RCC without disease progression compared with interferon alone, the company said.

"The AVOREN study has shown us that Avastin is an effective and safe treatment for kidney cancer," said Bernard Escudier, head of the Immunotherapy and Innovative Therapy Unit, Institut Gustave-Roussy, Paris, and principal investigator. "The drug offers new therapeutic options in advanced kidney cancer, where chemotherapy and radiotherapy are not as effective as in other cancers."

Kidney cancer is the fourth cancer type in which Avastin has demonstrated survival benefits, the company said. Data from the comprehensive Avastin cancer clinical development program have resulted in approvals in colorectal, breast, and lung.

The AVOREN study is a randomized, controlled, double-blind phase III study that included 649 patients from 101 study sites across 18 countries, the company said. Treatment consisted of either Avastin and interferon alpha-2a or placebo and interferon alpha-2a, a standard of care in advanced kidney cancer.

Trial data demonstrated the following information. By adding Avastin to IFN: progression free survival was almost doubled from a median of 5.4 to 10.2 months; tumor response was increased from 12.8 percent with interferon alone to 31.4 percent when Avastin was added; dose-reduction of IFN did not appear to affect the efficacy of the combination of Avastin (based on PFS event free rates over time, as shown by a sub-group analysis); the study also showed a trend towards improved overall survival; however, the survival data are still pending.

An interim analysis of the trial was performed in December 2006 and the benefits provided by Avastin were so positive that the Drug Safety Monitoring Board recommended that the trial was unblinded and participants were offered treatment with Avastin, the company said. The study demonstrated, for the first time that Avastin also is beneficial in combination with an immunotherapeutic, the class of drugs to which IFN belongs.

Veridex, LLC of Warren, N.J., said FDA granted an expanded clearance for the CellSearch System as an aid in the monitoring of metastatic colorectal cancer.

CellSearch is approved for monitoring metastatic breast cancer, the company said.

The system identifies and counts circulating tumor cells in a blood sample to predict progression-free survival and overall survival in metastatic colorectal or breast cancer, and can do so earlier than the standard of care, the company said. The results of serial testing for CTCs with the CellSearchSystem, in conjunction with other clinical methods for monitoring, would assess disease progression, thereby guiding more informed care decisions earlier.

"CellSearch will have a very positive impact on the care of the patients, in the same way it has positively impacted the care of our patients with metastatic breast cancer over the last year," said Ravi Patel of the Comprehensive Blood and Cancer Center in Bakersfield, Calif., which will become the first clinical site in the U.S. to offer the test under the new indication.

A multi-center clinical trial was conducted to validate the expanded clearance for CellSearch, the company said. The study, which took place in 55 clinical centers in the U.S. and Europe, involved 430 metastatic colorectal patients about to enter first- or second-line therapy. Data showed that with less than three CTCs at baseline, survival rates were better versus with more than three CTCs--an overall finding consistent for metastatic breast cancer, the company said. Data also showed that CTCs are a strong independent predictor of progression-free survival and overall survival, and that the combination of CTC analysis and radiological assessment may provide the most accurate assessment of prognosis.

The CellSearch test uses antibodies that are joined

to antibody particles, called ferrofluid, the company said. The antibody/ferrofluid combinations attach to CTCs. Powerful magnets then pull the CTCs out of the blood sample. They are then stained with additional biomolecules and chemicals so that they can be positively identified as CTCs. The CellSearch test differs from the standard of care because it can be used much earlier than traditional imaging, such as CT scans, and is not subject to the variation observed with other blood tests, called serum tumor markers, the company said.

Clinical Trials:

Allos Begins Phase I Trial Of RH1 In Tumors, Lymphoma

(Continued from page 1)

chemotherapeutic agent RH1 in advanced solid tumors or non-Hodgkin's lymphoma.

RH1, a small molecule chemotherapeutic agent, is bioactivated by the enzyme DT-diaphorase, which is over-expressed in tumors, including lung, colon, breast and liver tumors, the company said.

In the 60-patient study, treatment will consist of a three-hour intravenous infusion of RH1 administered once every 21 days, the company said. Starting doses of RH1 at 1.5 mg/m2 will be administered, with dose escalation in subsequent cohorts based on toxicity.

The objective is the maximum tolerated dose, recommended phase II dose and safety profile of RH1. Three to six patients will be enrolled per cohort. An expanded cohort of up to 24 evaluable patients who have tumor types with a high likelihood of DTD over-expression will be recruited to explore markers of anticancer activity. D. Ross Camidge, assistant professor of medical oncology at the University of Colorado Cancer Center, is study chairman, the company said.

AstraZeneca Canada Inc. of Toronto said Can-Am HIFU, a prostate cancer treatment center, will conduct a REB/Health Canada approved clinical trial for localized prostate cancer.

The study objective is to supplement research findings on safety and efficacy of HIFU therapy for the disease, the company said. The trial will measure both the biochemical cure rates and the biopsy-proven cure rates at one year.

The study will be led by Jack Barkin; Laurence Klotz,; Sender Herschorn, Neil Fleshner, Michael Robinette, Antonio Finelli, and Sidney Radomski, all Can-Am HIFU urologists.

"Data on HIFU are from studies conducted in other countries," said Barkin, chief of staff, Humber River Regional Hospital and director of Can-Am HIFU. "As more patients are considering HIFU as an alternative treatment option for prostate cancer, we recognize the need to build Canadian data on HIFU therapy."

HIFU has been used in several countries to treat localized prostate cancer and benign prostatic hyperplasia, the company said. The therapy uses ultrasound energy to heat and destroy specifically targeted areas of the prostate. HIFU was approved for use in the treatment of prostate cancer in Canada in June 2005. Can-Am HIFU urologists have been treating patients from Canada and abroad on an out-patient basis since March 2006. The Sonablate 500 is undergoing clinical trials in the U.S. and has not been approved for U.S. marketing by FDA, the company said.

Can-Am HIFU is a Canadian entity of USHIFU, LLC of Toronto.

Cleveland Clinic and Riverain Medical said it has begun the first study in an ongoing program to determine whether the OnGuard chest X-ray CAD, or computer-aided detection, can improve early detection of lung cancer.

"Developing early detection methods is a key to improving treatment of lung cancer," said Micheal Phillips, section head of Imaging Sciences, Department of Diagnostic Radiology, Cleveland Clinic. "As it stands now, treatment options are limited because identifying malignant lung tumors in their early stage is so difficult."

The evaluation of X-Ray CAD is funded by a grant from the State of Ohio, the groups said. Moulay Meziane is the principal investigator for the five-year 9,000-patient study.

Chest X-ray CAD software identifies regions of interest (actionable/suspicious pulmonary nodules) in the X-ray, and circles them for further analysis, the groups said. The radiologist is then able to review the areas and determine whether additional follow-up is needed for further evaluation/diagnosis.

In clinical trials, the CAD technology identified 16 percent more 9-15 mm solitary pulmonary nodules that were early stage (1A) lung cancer than would have otherwise detected without CAD, the groups said. OnGuard is the only FDA-PMA approved chest X-ray CAD product on the market, the groups said.

Cleveland Clinic Foundation and Riverain Medical, along with Wright State University and University Hospitals Health System, have formed the Early Lung

Disease Detection Alliance, a multidisciplinary research and commercialization program that will develop, test (through clinical trials), and bring to market new image-analysis systems for the early detection of lung cancer and other lung diseases, the groups said. This computer-aided detection system will be applied to the most widely available and used imaging exam, the chest x-ray. The goal is to advance the early detection of lung cancer and other diseases and also accelerate the commercialization of computer-aided detection, image interpretation, and multidisciplinary applications of computer science and medical diagnostics.

Hana Biosciences (NASDAQ: HNAB) of South San Francisco said dosing of two patients has begun in a phase II trial of Marqibo (vincristine sulfate injection, Optisome) for metastatic malignant uveal melanoma.

The study would assess the efficacy of the drug, the company said. Secondary objectives are safety and antitumor activity of Marqibo as determined by response duration, time to progression, and overall survival. The population is defined as adults with uveal melanoma and confirmed metastatic disease that is untreated or that has progressed following one prior therapy. Hana said enrollment would be up to 30 and is being conducted at MD Anderson Cancer Center.

In the phase I trial, treatment with Marqibo for metastatic melanoma originating in the eye demonstrated promising single-agent activity, said Patrick Hwu, chairman, Department Melanoma Medical Oncology at M. D. Anderson Cancer Center. An objective response rate (complete response plus partial response) of 13 percent and stable disease rate of 20 percent was achieved among 15 patients with histologically confirmed, surgically non-resectable metastatic cutaneous, mucosal, or uveal melanoma. One of four subjects with uveal melanoma metastatic to the lung achieved a complete response. The agent was generally well tolerated, Hwu said.

"Metastatic uveal melanoma generally does not respond to systemic chemotherapy and has limited treatment options," said Agop Bedikian, professor, Department of Melanoma Medical Oncology at M.D. Anderson , and principal investigator. "We are encouraged by the results we have seen with Marqibo and believe that it will benefit the population."

Marqibo, an Optisomal formulation of vincristine, has shown anti-cancer activity in acute lymphoblastic leukemia, non-Hodgkin's lymphoma, and melanoma in clinical trials, the company said. Vincristine is FDA-approved as a single agent and in combination regimens for hematologic malignancies such as lymphomas and leukemias. Vincristine, a microtubule inhibitor, kills cancer cells when they enter a point in the cell cycle, and its efficacy is concentration-and exposure duration-dependent. Marqibo extends the circulation time of vincristine in the bloodstream, increase targeting of the drug to malignant cells, and enhance exposure duration at the site of the disease. Unlike regular vincristine, Marqibo is dosed based on body surface area without the need to limit the dose to avoid neurotoxiciites, the company said.

Optisomes are sphingomyelin/cholesterol-based nanoparticles that encapsulate cell cycle-specific chemotherapeutics for improved efficacy with reduced toxicity, the company said. Optisomes are approximately 100 nanometers in diameter and able to encapsulate and transport cancer drugs preferentially to tumor sites. Their sphingomyelin-cholesterol composition is well suited to cell cycle-specific agents such as vincristine, vinorelbine and Topotecan, the company said.

Hana said its Optisome pipeline includes Marqibo (vincristine), Alocrest (vinorelbine) and Brakiva (topotecan).

Peregrine Pharmaceuticals Inc. (NASDAQ: PPHM) of Boston and Tustin, Calif., said preclinical data presented showed that its anti-VEGF antibody R84 was as effective as Avastin (bevacizumab) in inhibiting tumor growth in a mouse model of human breast cancer.

R84 is a selective, fully human monoclonal antibody that blocks the cancer-promoting agent vascular endothelial growth factor, the company said. The product blocks VEGF from binding only to VEGF receptor 2, while non-selective agents such as Avastin block binding to both VEGFR2 and VEGF receptor 1.

R84 is a product of the collaboration between Peregrine and antibody developer Affitech AS of Oslo, the company said.

The study treated tumor-bearing animals with R84, Avastin, or a placebo in an orthotopic model of breast cancer, said Rolf Brekken, assistant professor of surgery and pharmacology and Effie Marie Cain Scholar in Angiogenesis Research at UT Southwestern Medical Center, and an advisor to Peregrine. Treatment with R84 reduced the growth of well-established breast tumors by 55 percent, equivalent to the reduction achieved with Avastin. R84 and Avastin were equally effective at controlling tumor growth in a preclinical model of sarcoma. In every preclinical tumor model evaluated thus far, the anti-tumor activity of R84 has

been comparable to that of Avastin, the company said.

The study results also showed that tumor-associated macrophages, immune system cells found in tumors, are reduced after R84 therapy, the company said. Tumor-associated macrophages are associated with poor prognosis as the cells are linked to increased angiogenesis and metastasis. In addition, the data showed that when given for a prolonged period, R84 decreased microvessel density and expression of VEGFR2, demonstrating that the antibody is acting to reduce VEGF-induced angiogenesis in tumor tissue.

Peregrine in association with Affitech has filed a patent application for R84 with the U.S. Patent and Trademark Office to preserve the right of patent protection in the U.S., all member countries of the European Union, the company said.

In another development, Peregrine said its phase II protocol bavituximab in combination with the chemotherapy drug docetaxel has been approved by the Drug Agency of the Ministry of Labor, Health and Social Affairs of Georgia for metastatic breast cancer.

The open label, multi-center safety and efficacy trial is expected to begin enrollment by early next year. The primary objective is to assess the overall response rate to the combination of drugs, the company said. Secondary objectives include measuring time to tumor progression, duration of response, overall survival and safety parameters. In the two-stage design, up to 15 patients will be enrolled. The study will then be expanded up to a total of 46.

Tumor response will be evaluated using Response Evaluation Criteria in Solid Tumors parameters. The trial is being conducted according to International Conference on Harmonization and Good Clinical Practices standards, the company said.

In a phase lb trial in advanced cancer, bavituximab plus chemotherapy appeared to have a safety profile consistent with chemotherapy alone and showed positive signs of clinical activity, achieving objective response or disease stabilization in 50 percent of the evaluable patients, the company said. A protocol for a phase II trial of bavituximab in combination with paclitaxel and carboplatin in metastatic breast cancer is undergoing regulatory review in India. A protocol for a phase II trial of bavituximab in combination with paclitaxel and carboplatin in non-small cell lung cancer also is under regulatory review in India. Bavituximab is in clinical trials in the U.S. for advanced solid tumors and in patients co-infected with HCV and HIV.

Synta Pharmaceuticals Corp. (NASDAQ: SNTA) of Lexington, Mass., said treatment has begun in the Synta Metastatic Melanoma Elesclomol Trial, or SYMMETRY, which is a global, phase III study to evaluate the safety and efficacy of elesclomol in stage IV metastatic melanoma.

Synta also said it has completed the Special Protocol Assessment process, reaching agreement with FDA on the design, conduct, and planned analyses of the trial.

Elesclomol is a small molecule, first-in-class drug candidate, discovered and developed by Synta, that elevates the level of oxidative stress of cancer cells beyond a breaking point, inducing apoptosis, the company said.

In a phase II double-blind, randomized, two-center trial in metastatic melanoma, treatment with elesclomol doubled median progression-free survival, achieving the primary endpoint of the study to statistical significance, the company said.

The 630 patient-trial will be randomized (1:1) to elesclomol (213 mg/m ^{2}) plus paclitaxel (80 mg/m^2) or paclitaxel alone (80 mg/m^2) and will receive three weekly treatments and one week without treatment per each four week cycle, the company said. Stratification will be made according to LDH levels, M-grade status and prior treatment history. Responses will be assessed using standard RECIST criteria at baseline and at a minimum every other cycle, with radiology scans being assessed by independent, blinded, reviewers at a central site.

The control arm treatment, the combination arm treatment, the doses, the schedule, and the primary endpoint—progression free survival—are the same as in the prior phase IIb trial, the company said.

Following, two additional analyses for OS are planned: a second interim analysis and a third and final OS analysis.

Deals & Collaborations:

Beckman To Buy Dako's Flow Cytometry Business

Beckman Coulter Inc. (NYSE: BEC) of Fullerton, Calif., and **Dako Denmark A/S** of Glostrup said Beckman Coulter will acquire the Dako research flow cytometry instrumentation business of Fort Collins, Colo.

"We are adding the Dako MoFlo XDP high-performance sorter, the gold standard for cell sorting, and the nine-color CyAn research flow cytometer to our existing portfolio of cytometry instruments, allowing

us to offer a more comprehensive range of research solutions to our customers," said Scott Garrett, president and CEO of Beckman Coulter.

"The action reinforces our intent to create a more focused business in anatomic pathology and tissue-based cancer diagnostics," said Patrik Dahlen, Dako president.

The Dako flow cytometry instrument business workforce of 200 includes sales, marketing, research, manufacturing and administrative personnel, the companies said. Flow cytometry is used to analyze cells in blood and other fluids for both research applications and diagnosis of diseases such as leukemia, lymphoma and HIV.

The transaction is expected to close by the end of the year, the companies said.

Inverness Medical Innovations Inc. (AMEX: IMA) of Waltham, Mass., said it has entered into a definitive agreement to acquire **ParadigmHealth Inc.** of New Jersey, a provider and integrator of care and disease management services for the acutely ill and the clinically complex, including neonatal intensive care and oncology.

The transaction is structured as an all cash deal, with a purchase price of $230 million, the company said.

Rigel Pharmaceuticals Inc. (NASDAQ: RIGL) of South San Francisco said that Merck Serono, a division of Merck KGaA, has exercised its option to add the Japanese territory to its Aurora kinase collaboration that includes R763/AS703569.

In exchange for the extended development and marketing rights, Rigel said it will receive a $3 million payment.

R763/AS703569 is an oral inhibitor of Aurora kinases and has exhibited anti-tumor activity against a range of cancer cell lines, the company said. Three phase I trials with the agent, sponsored by Merck Serono, have been initiated and are ongoing in solid tumors and leukemia.

Oncology Management:

CyberKnife Has Treated 4,000 Lung Cancer Patients

Accuray Inc. (NASDAQ: ARAY) of Sunnyvale, Calif., said its CyberKnife Robotic Radiosurgery System has treated 4,000 lung cancer patients.

The company also said 40,000 were treated with CyberKnife radiosurgery for tumors throughout the body.

Treatment growth is due in part to the increasing availability of the Accuray lung cancer treatment at CyberKnife centers, the company said. Centers offer treatment that include the Synchrony Respiratory Tracking System, which synchronizes radiation beam delivery with the motion of the tumor, and the Xsight Lung Tracking System, which uses internal anatomy to track lung tumors non-invasively. The number of treatments will increase with the initiation of the M. D. Anderson clinical lung study, the company said.

The CyberKnife Robotic Radiosurgery System uses continual image guidance technology and computer controlled robotic mobility, the CyberKnife System automatically tracks, detects and corrects for tumor and patient movement in real-time, the company said. This enables the CyberKnife System to deliver high-dose radiation with pinpoint precision, which minimizes damage to surrounding healthy tissue and eliminates the need for invasive head or body stabilization frames, the company said.

Cedara Software of Toronto said its imaging service grid and a specialized version of I-Response have been integrated with the NCI National Cancer Imaging Archive.

The NCIA is a searchable repository of in vivo cancer images acquired during clinical trials, the company said. The Cedara Software technology provides a central clinical viewer to review and analyze NCIA data.

"Centralized image access, review and analysis could reduce the amount of resources and time required to perform image evaluation for a variety of clinical trials," said Eliot Siegel, professor of diagnostic radiology at the University of Maryland In Vivo Imaging Workspace, part of the NCI Cancer Biomedical Informatics Grid.

The imaging service grid is configured as a scalable 64-bit back-end solution that is integrated with the archive component from NCIA, the company said. The grid can be deployed as a standalone server that serves images to several clients, or scaled to a server-farm deployment that can serve images to hundreds of clients, as well as support load-balancing of the clients. It also can be connected and serve images to any viewer, the company said.

The I-Response viewer establishes an HTTP request with the imaging service grid and allows the employment of measurement tools found in I-Response

on the studies, the company said. The distributed processing viewer contains image analysis tools that enable researchers to evaluate and quantify images obtained during clinical trials. I-Response supports multiple modalities and operates with imaging equipment from different manufacturers, the company said.

Cedara Software is a Merge Healthcare company.

Oncology Metrics of Dallas-Fort Worth, Texas, announced the launch of the second in its series of Oncology Metrics National Indices that track trends in the diagnosis, treatment and management of cancer.

The OMNIs, conceived by Oncology Metrics and designed to shine a spotlight on 12 key areas of cancer care, (HER2 Testing, ONCOTYPE DX are examples of other OMNIs in development) have been vetted by an advisory board comprised of community oncologists led by Dean Gesme, Director of Clinical Measurement for Oncology Metrics.

"The OMNI is an index, not a benchmark," Gesme said. "There really isn't a right value of any individual OMNI; rather, through the monitoring of and publication of trends in the indices, our goal is to stimulate dialogue and debate amongst the key stakeholders in the oncology industry. We hope this dialogue will help enhance the quality of cancer care."

According to the company, electronic medical records in oncology have made it possible to develop analytic tools to add objective data to the discourse on practice patterns and to track the changes that occur in the patterns of care.

The index is designed to measure the rate at which cancer patients are staged and recorded in a searchable field in the electronic medical record, the company said. Past studies have shown most patients are staged in the paper chart but that in electronic charting, staging is often found in unstructured areas rendering it difficult to analyze systematically.

The staging index is described on the company's website, www.oncomet.com.

OneOncology Inc. of Orlando, Fla., said hundreds of community oncologists, representing more than $1.47 billion in annual oncology drug purchasing commitments, have registered for the OneOncology first electronic negotiation event to be held Dec. 11.

The milestone follows the completion of the company two-week Practice Freedom Tour during which doctors, practice administrators, pharmacy managers, oncology nurses and others met with OneOncology executives and discussed how to shift market power and lower drug pricing to community oncologists by combining purchasing power, the company said.

"The tour gave us a chance to address misperceptions about OneOncology and present the facts on how we are helping community oncologists overcome the challenge of shrinking drug margins," said Ben Favret, vice president of OneOncology. Favret said he traveled to six cities, led a live Web cast and posted a daily blog at www.practicefreedom.org about his experiences during the two-week Practice Freedom Tour.

"Practices responded favorably as we shared information about how our electronic negotiation technology brings competition and transparency to oncology drug distribution," said Favret.

At the Dec. 11 event, orders for individual drugs will be aggregated from practices across the country, and then distributors will bid to fill the orders at the lowest price during an online negotiation, the company said. Similar technology in other industries has been proven to lower prices 3-35 percent.

OneOncology said it is not a distributor, not a group purchasing organization and not an oncology practice. OneOncology said it is an impartial market maker dedicated to bring lower prices and greater competition to the oncology drug distribution.

Pharsight Corp. (BULLETIN BOARD: PHRS) of Mountain View, Calif., said its Strategic Consulting Services Group is using a quantitative disease model developed by FDA for non-small cell lung cancer to support an oncology drug development program.

FDA's publicly available disease model in NSCLC is being used to perform simulations of expected survival based on tumor shrinkage, the company said. Pharsight said the simulations would assist with oncology development program decisions, including optimized dose selection and improved design of survival trials.

Pharsight said its collective modeling and simulation experience in oncology includes longitudinal exposure-response modeling for labeling decisions and test dosing strategies, allometric projections, and work with mechanisms.

FDA has developed quantitative drug-disease models based on the literature and clinical trial data from sponsor submissions for drug approval, the company said. FDA does not release proprietary source data from sponsors used to develop and validate the models, but the agency publicly shares and tests the models that it has developed in important disease areas.