THE CANCER LETTER

Vol. 35 No. 9
March 6, 2009

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

NCI Prepares To Dispense A Torrent Of New Money For Cancer Research

By Kirsten Boyd Goldberg

As they compete for a share of the sudden multi-billion-dollar influx of funding for research and construction, NCI grantees say they are grateful, but overwhelmed.

"There's little doubt that these increases will provide an enormous flexibility and an enormous opportunity; on the other hand, it's a little like trying to drink out of a fire hose," said Robert Young, chancellor of Fox Chase Cancer Center.

Young, chairman of the NCI Board of Scientific Advisors, was among the advisors who made it to Washington, D.C., during a snowstorm March

(Continued to page 2)

In the Cancer Centers:

Hollings Cancer Center At MUSC Wins NCI Cancer Center Designation, $7M Grant

HOLLINGS CANCER CENTER at the Medical University of South Carolina has attained NCI cancer center designation, a distinction held by only 63 other cancer centers in the U.S. The designation, through a Cancer Center Support Grant, includes more than $7 million in funding.

"We are honored and proud to have earned this recognition," said Center Director **Andrew Kraft**. "It is a distinction earned over many years through collaboration and innovation by dedicated researchers, clinicians, and staff throughout Hollings Cancer Center and MUSC. By sharing what we know with other cancer centers and practices throughout our state, we can step up our war on cancer in South Carolina and beyond. Our citizens don't have to leave the state to find the most advanced research and protocols from an NCI center—we have one right here in our back yard."

Former **Sen. Ernest "Fritz" Hollings**, for whom the cancer center was named in 1993, called the designation "a true milestone for the Medical University of South Carolina." **Sen. Lindsey Graham** called the designation a "game-changer" for the thousands of South Carolinians with cancer.

"Cancer is one of the leading causes of death in the nation and practically every family in our state has been impacted by this horrible disease. The Hollings Cancer Center will now take its place among an elite group of institutions in the major leagues of cancer research," Graham said. "The NCI designation only comes to the best and brightest. It is a compliment to

(Continued to page 7)

NCI Director: Stimulus Science Should Offer "Exciting Stories"

(Continued from page 1)

2 to hear NCI Director John Niederhuber discuss the institute's plans for managing the new money.

Scientists will likely have very little time to prepare grant applications in response to new Requests for Applications, said BSA member James Heath, professor of chemistry at California Institute of Technology. Between the time the RFAs come out and the proposed due dates, "I couldn't quite calculate the number of hours," he said.

"You mean you haven't been writing already?" Niederhuber replied.

However, the NCI director said he was in no position to be specific. "I need to stress for you that this is a work in progress. No decisions have been finalized," Niederhuber said of the rapidly-evolving spending plans at NIH and NCI.

"The status of the stimulus funding is that we contributed to a funding plan for NIH and that funding plan is being reviewed at the department," he said. "Until that is completed, we really don't have any concrete information about how this will be distributed across the institutes."

In addition to stimulus funds, under the FY2009 omnibus appropriation bill, NCI would receive $4.96 billion, an increase of $138 million or nearly 3 percent, compared to FY08. The measure was passed by the House, but stalled in the Senate this week as a result of Republican opposition to a massive number of earmarks. NIH is being funded through continuing resolutions.

NCI Goal: Move Money Out In 2009

NCI will try to get the majority of its stimulus funds—expected to be around $1.26 billion—into the coffers of grantees before the end of this year, Niederhuber said to the board.

"If, in fact, we really have to report out on Sept. 30, 2010, that all money has been spent—if that requirement sticks—then we've got to, as an institute, move as much of this out in 2009 as we can in order to have an impact," Niederhuber said. "It's important to get as much money out the door to give you a chance to work with it."

The institute's budget staff is running simulations of the impact of funding the first two years of four-year grants with stimulus funds and then using the regular appropriation to fund the remaining years of these grants, he said.

"It's a large amount of resources, and it is a challenge in terms of management, to work with a system that isn't quite used to the way we do science," Niederhuber said to the BSA. "But we really are working hard to do this in an effective way to support the best scientific opportunities, projects with the broadest impact, and work that can be accomplished in a few years."

The BSA gave unofficial approval to two RFA concepts that would use stimulus money. One would fund administrative supplements for research collaborations and the other would support two-year grants to stimulate research on vaccines against viruses implicated in HIV-associated malignancies. The board wasn't asked to vote on the concepts, but the members' comments favored NCI moving forward with the RFAs. (See story, page X).

In deciding how to use the stimulus funds, NIH officials think back to the post-doubling years, when Congress held the NIH budget flat, Niederhuber said. "We don't want to go back to 2003 and 2004, when we were constantly having to defend against the statement, 'We already doubled your budget. Why do you need more resources?'" he said.

"As I told my Executive Committee, if the ideas that we put forward aren't exciting enough and aren't stimulating enough to our science, and aren't stories that will be exciting to the legislature, and in the end, we have done a great job of getting dollars out the door, but in 2011 and 2012, that [money] isn't in our base, then as the leadership of NCI, we have failed," Niederhuber said.

THE CANCER LETTER

® The Cancer Letter is a registered trademark.

Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg

Editorial: 202-362-1809 Fax: 202-379-1787
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: www.cancerletter.com

Subscription $385 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

"We have that principle sort of tattooed up here in trying to guide our decisions."

Funding Mechanisms and Budget Modeling

Among the mechanisms NCI can use for the stimulus funding:

—**Select from reviewed and new R01s or other research project grants**, picking "those things that are new and meritorious and could make a significant difference in science," and could be completed in two years.

The problem is that most good science doesn't end in two years, Niederhuber said. "A great experiment generates 20 more experiments in our labs, if we are successful," he said. "What I would like you to take away from this discussion is that I understand the complexity for the researcher and the associate dean for research."

Even though NCI has to keep its regular appropriations separate from the stimulus funds, the budget office is exploring how it could adhere to the requirements while using stimulus funds for the first two years of four-year grants, Niederhuber said.

"We are trying to think of innovative ways in which we can gamble a bit on our out-year obligations and fund as much of this as we legitimately can without overdoing our risk, in terms of three- and four-year commitments, rather than just two-year commitments," he said.

"I hope that you will have confidence that I and my team recognize that as much as we can, we want the combination of these resources to do what we normally do," he said. Grant applications "at the higher end of risk" might only receive two-year awards, he said.

"We probably have just in 2009, for example, about 240 or 250 grants that would fall, say, above the 18th percentile, to give you some perspective, or between the 18th to 25th percentile," he said. "Don't write that down, but that's to give you a sense of what we might be looking at in terms of numbers.

"We are trying to work on models where we can look at out-years and say, 'We can take this amount of red ink and cover that,"" Niederhuber said. "It's important for us to model what is the worst risk we can take in order to obligate more in terms of four-year and five-year grants. This is just our thinking, please don't take it further.

"What about the new investigator awards?" Niederhuber said. "It doesn't make sense to fund new investigator awards for two years. So we model it as four-year, though we might use stimulus money up front.

"You have to also think about the number of grants. It's not just the dollars; there is going to be increased competition. If we fund more grants now for four years, 90 percent will come back in for recompetition."

BSA member Mary Hendrix, president and scientific director of the Children's Memorial Research Center at the Lurie Comprehensive Cancer Center, asked whether stimulus funds could be used to restore "some of the cuts that current R01 grants sustain every year in competitive renewal."

"In stimulus funds that is clearly a no-no," Niederhuber said. "The stimulus dollars are absolutely not to be used to make up for losses. We are going to have to show how they are directed to new science, hiring new people." NCI's annual budget could be used for that purpose, he said.

"If we got the stimulus, but not the appropriation increase, or a decrease in appropriations, it would have been a disaster," Niederhuber said. "I know the pain of the decreases, but I also know when I talk to the grantee community, they say, not at expense of new grants. They will say to be I don't care if its two years, just gave it to me. If I had an R01 or two in my pocket, it made it better for me in the dean's or chairman's office.

—**Accelerate the tempo of ongoing science through carefully targeted grant supplements**.

"We are planning on a daily basis how we might accelerate science through projects that were perhaps on the investigator's list to do, perhaps a specific aim that got dropped because of the funding, a project that was taken out of a SPORE," Niederhuber said. "We are not simply putting money in to make up that difference, but we are putting money in to do new things."

—**New programs that fit the goals of the stimulus act**, including new NIH and NCI RFAs.

The NIH Challenge Grant announcement was posted March 4 at http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-09-003.html. Also, a web site for Challenge Grant information opened at http://grants.nih.gov/grants/funding/challenge_award/.

Challenge Grant applications are due April 27, with peer review in June/July and award on Sept. 30. According to the announcement, NIH will set aside $200 million to fund "200 or more" two-year grants of $500,000 a year total costs. Grants also may be eligible for comparative effectiveness research funds. The announcement describes 15 "challenge areas" of emphasis for the grants.

Grantees will have to comply with rigorous reporting requirements, Niederhuber said. "The

accountability and transparency of how these dollars in the stimulus are used are going to be unprecedented for us," he said. "They are going to be given to us by individuals who perhaps aren't so understanding of how we fund and do science. So we are going to have accountability issues that are going to be tough on us to administer and require a great deal of cooperation between the institutes that we fund and the individual grantee."

—**Construction and shared instrumentation**: NIH will have $1 billion for extramural construction and $300 million for extramural share instrumentation and other capital equipment.

Universities are already getting proposals ready to compete, Niederhuber said. "I'm sure that if those projects are 'shovel-ready,' you will have a much better opportunity to compete," he said. "There probably aren't that many construction projects at universities that have gone through all the approvals process, have the architectural work complete, and are literally ready to go into the ground, but with the economy changing, there are several projects I'm aware of where the institutions have pulled back. I suspect a lot of this, because of the time frame, will probably be spent on renovation of existing buildings."

Plans are being made for use of the intramural construction and renovation on the NIH campus, Niederhuber said. Several institute directors are hoping some funds will be used to complete the renovation of Building 10, which is centrally located on the campus, he said.

—**Comparative Effectiveness Research**: NIH will have $400 million for comparative effectiveness research. HHS has another $400 million and the Agency for Healthcare Research and Quality will have $700 million for this research. Niederhuber is a member of an internal NIH committee on CER. Specific plans for these funds haven't been finalized, he said.

Other stimulus funding of potential interest to NIH grantees includes:

—$2 billion in the HHS Office of National Coordinator for Health Information Technology. These funds must "remain available until expended."

—$1 billion in a Prevention and Wellness Fund administered by the HHS Secretary's office, including $650 million to carry out evidence-based clinical and community-based prevention and wellness strategies that deliver specific, measurable health outcomes that address chronic disease rates. CDC and NIH officials are currently wresting over use of these funds, sources said.

ASCO Weighs In On Stimulus Funds

On Feb. 24, the American Society of Clinical Oncology sent a letter to Niederhuber with recommendations on use of the stimulus funding.

ASCO suggested that NCI should:

—Increase per-case payments for NCI-funded clinical trials.

—Provide supplemental funding to NCI's research infrastructure.

—Increase grants for researcher training.

—Fund promising new translational research.

At a briefing Feb. 17, Acting NIH Director Raynard Kington said stimulus funds might not be appropriate to support a clinical trial due to the two-year limit on the funds (The Cancer Letter, Feb. 20). However, in the letter, ASCO President Richard Schilsky wrote that using stimulus funds to increase per-case payments for current NCI-supported clinical trials would support the hiring of research staff, allow for faster completion of trials, and provide the data to bring products to market.

Following is the text of the letter to Niederhuber:

The American Society of Clinical Oncology (ASCO) is very pleased that Congress provided an additional $10 billion for the National Institutes of Health, including approximately $1.2 billion for NCI, in the American Recovery and Reinvestment Act (H.R. 1). ASCO supported the legislation and Senator Specter's amendment because of the vital role of NIH and NCI in our country's cancer research enterprise.

It is clear from comments made by NIH Acting Director Raynard Kington, MD, PhD, that NIH is taking very seriously its responsibility to use this funding to stimulate the economy and plans unprecedented public accountability for how the funds are used. We fully support these efforts. NCI's existing matrix of extramural programs allows the Institute to quickly disburse the stimulus funds to communities throughout the U.S. Existing research programs can use the funding to employ research personnel and purchase state-of-the-art equipment necessary to energize the clinical and translational research enterprise. This will translate directly to increased job opportunities for young investigators, research nurses, and research staff. These are the types of positions that will help bring about lasting growth in communities throughout the U.S.

We support the use of a portion of the stimulus funding to increase the number of investigator-initiated research project grants that are funded by NCI. However, as you work with Dr. Kington on implementation plans for the remaining funding, we wanted to share with you

our thoughts regarding priorities for its use.

Increase Per-Case Payments for NCI-Funded Clinical Trials – NCI has a robust extramural mechanism to provide access to its trials throughout the US in most every community in which cancer care is offered. Increasing the per-case reimbursements investigators receive to cover the costs of conducting clinical trials will directly support the investigators and research staff who conduct those clinical trials and result in greater participation, thereby speeding the answers these trials are helping provide. NCI will also be able to easily track the impact of this policy by monitoring clinical trials accrual. ASCO firmly believes that this stimulus funding should be used to support clinical research and providing it to trials that are already open in the community setting is the best mechanism to do that. NCI has not increased the $2000 per-case payment that it makes to clinical investigators who enroll patients in NCI-funded trials since 2000. Even at that time, studies done by ASCO and C-Change demonstrated that this payment far under-funded the costs that research sites incur by participating in NCI-funded trials. NCI has developed a process for increasing reimbursement for high-complexity trials. ASCO supports this effort, but believes that the base capitation rate should also be increased. NCI should use the additional funding provided by HR 1 to both increase the $2000 per-case reimbursement and provide additional funding to complex trials. Such an infusion of funds will permit immediate hiring of research staff and will translate into more rapid completion of clinical trials. Many of these will provide the data necessary to bring new products to market.

Provide Supplemental Funding to NCI Research Infrastructure – NCI's standing infrastructure of research institutions and community-based research sites throughout the country enable NCI to demonstrate return on investment for clinical and translational research. Existing grantees operate across the full continuum of research – from SPOREs to cancer centers to cooperative groups to CCOPs, NCCCP, and CTSU sites. NCI should use the stimulus funds to provide supplements to existing grantees to support promising areas of research, training, research staff, and equipment. Priority should be given to supplemental support of personnel-driven core facilities such as clinical trials offices, statistical centers, and informatics facilities.

Increase Grants for Researcher Training – NCI provides critical funds to our training institutions to ensure that we are continually developing our next generation of investigators. The economic environment is making it increasingly difficult for these institutions to continue this vital mission. Coupled with the growing concern about whether we will have an adequate workforce in the coming years, this is making trainees reconsider pursuing a career as a clinician investigator. Increasing funds in this area would help ensure that we continue to bring the best minds to the field of translational and clinical research.

Fund Promising New Translational Research – NCI is currently in the process of prioritizing translational research opportunities with the goal of accelerating this important research. With the tremendous advances we are unlocking with our increased understanding of the molecular basis for cancer, there are numerous, exciting opportunities to advance into the clinical setting. NCI could accomplish this by bolstering our existing infrastructure, as well as launching new funding mechanisms to rapidly accelerate the clinical development of new drugs and diagnostics.

We appreciate your leadership during this tumultuous time. We are eager to work with NCI in whatever way we can to ensure the best use of these vital funds and, ultimately, the greatest impact on the quality of cancer care.

NCI Programs:

Institute Plans Two New RFAs For Use Of Stimulus Funds

By Kirsten Boyd Goldberg

NCI plans to issue two Requests for Applications that would use economic stimulus funds to support research collaborations and research on vaccines against viruses implicated in HIV-associated malignancies.

The NCI Board of Scientific Advisors wasn't asked to vote on the concepts, as normally would be the institute's practice, but the members' comments at a meeting March 2 favored NCI moving forward with the RFAs.

Dinah Singer, director of the NCI Division of Cancer Biology, said concepts for the two RFAs were being written before the stimulus bill was passed. "These are concepts we regard as 'shovel-ready,'" Singer said to the BSA.

—NCI Activities To Promote Research Collaborations has been an administrative supplement program with the Division of Cancer Biology for a number of years. It now would be open to any NCI grantee receiving the following awards: P01, P20, P25, R01, R33, R37, U01, U10, U19, or U54/56.

The supplements would support new multidisciplinary research collaborations across

the cancer research continuum. This would allow investigators to bring in new collaborators. Both the proposed project and the collaboration must be novel. All collaborators must be funded by peer reviewed mechanism. The collaborators who propose to work together must not have previously collaborated for the past five years.

The application is simple and short, Singer said. NCI would set aside $15 million of its stimulus funds over two years to support 12 to 15 new collaborations. Each supplement would provide $100,000 to $300,000 per year for up to two years.

Receipt date for applications will be April 15, with funding provided June 1.

BSA member Richard Schilsky, of University of Chicago, noted that P30 and P50 grants weren't on the list. Singer said those could be added, and that the focus of the supplements could be clinical and translational research if the projects fell within the time constraints.

BSA member Michael Caliguri said NCI should consider increasing the total amount dedicated to these supplements. "I could think of 10 of these that could come from our place alone," said Caliguri, director of the Ohio State University Comprehensive Cancer Center.

BSA member Curt Civin, associate dean for research, University of Maryland School of Medicine, asked whether NCI would consider increasing the amount of funding per award.

Singer said she "wouldn't be comfortable awarding more" than $300,000 per year as an administrative supplement, without competitive review.

—**Development of Vaccines Against HIV-Associated Malignancies or HIV Infections**, to stimulate research in either preventative or therapeutic vaccine development against HIV and HIV-associated viral malignancies. Some HIV-associated viruses include: KSHV/HHV8, EBV, HCV, MCPyV, and HPV types not in the current vaccine.

The goal of these two-year grants would be to stimulate research, not to develop vaccines, Singer said. BSA members noted the title should be changed to reflect the emphasis on stimulating research.

"There is almost no work going on addressing these viruses," Singer said. This area was recommended as a high priority by the AIDS Malignancy Working Group. The National Institute on Allergy and Infectious Diseases supports HIV vaccine research, but not vaccine research targeted to HIV-associated malignancies, Singer said.

NCI would fund this work with U01 cooperative agreement awards to allow NCI to monitor progress. Grants would be funded for $500,000 per year for two years. NCI would provide a total of $10 million a year for two years to fund 20 to 30 applications.

Caligiuri said the proposed funding of $1 million over two years is "a good amount of money."

NCI Director John Niederhuber said the institute would like to see applications for vaccines against the HIV-associated malignancies as well as against the causative viruses. The latter, he said, "is where the real progress can be made," but NCI would like to see a mix of proposals.

BSA Chairman Robert Young, chancellor of Fox Chase Cancer Center, said the board had "considerable enthusiasm" for the proposed RFAs, and that the concepts "might be nice examples of the way you address RFAs in the context of the stimulus package."

In Brief:

Kansas Gov. Kathleen Sebelius Nominated For HHS Secretary

PRESIDENT BARACK OBAMA nominated Kansas Gov. **Kathleen Sebelius** as his choice for secretary of the Department of Health and Human Services.

Sebelius served eight years as the Kansas insurance commissioner and was an early supporter of Obama in his presidential campaign. Senate confirmation is expected.

Obama also named **Nancy-Ann DeParle** to head the White House Office of Health Reform. DeParle was director of the Health Care Financing Administration in the Clinton administration and most recently was managing director for health care at CCMP Capital, a private equity fund.

EZEKIEL EMANUEL is on detail from NIH to the Office of Management and Budget, where he is a special advisor on health policy to OMB Director **Peter Orszag**. Emanuel is chairman of the Department of Bioethics at the NIH Clinical Center and brother of White House Chief of Staff **Rahm Emanuel**. He is working in the Eisenhower Executive Office Building.

PEANUTS AND CANCER PATIENTS: Because cancer patients with impaired immune systems are more likely to become severely ill from a Salmonella infection than others, NCI developed a new Fact Sheet, "Peanut Product Recall and Cancer Patients," to address the special concerns of cancer patients and their healthcare providers due to the contamination of products produced by the Peanut Corporation of America. Due to this

contamination, all peanut products produced by PCA on or after January 1, 2007, have been recalled. The fact sheet is posted at http://www.cancer.gov/cancertopics/factsheet/Support/peanut-recall.

For a searchable list of recalled products, visit http://www.accessdata.fda.gov/scripts/peanutbutterrecall/index.cfm.

In the Cancer Centers:

Ann Schwartz Named Interim President At Karmanos Center

(Continued from page 1)

the men and women who put in countless hours at this facility and recognition that the Hollings Cancer Center is among the best of the best in cancer research."

BARBARA ANN KARMANOS CANCER INSTITUTE and Karmanos Cancer Center boards of directors said **Ann Schwartz** was appointed interim president and CEO. Schwartz served as the associate center director for population sciences at Karmanos since 2002. Her research focuses on the genetics underlying lung cancer risk. Schwartz steps in as **John Ruckdeschel**, outgoing president and CEO, takes the job as director and CEO of the Nevada Cancer Institute (The Cancer Letter, Feb. 6). The Karmanos boards also named **Paul Broughton** as interim chief operating officer. Broughton served on both Karmanos boards through December 2007 and was a member of the institute's finance and compensation committees. Prior to his retirement, he was president and CEO of Harper Hospital and Children's Hospital of Michigan. . . . **DAVID SYMER**, head of the NCI epigenetics section, joined Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute, as an assistant professor and researcher in the Department of Molecular Virology, Immunology and Medical Genetics. He also is a practicing physician in the division of hematology and oncology; and an adjunct member of the department of biomedical informatics. Symer's research focuses on jumping genes, or transposons, in mammals. Transposons are unusual segments of DNA that can move to different positions within the genome of a single cell. Researchers believe that these tiny snippets, formerly known as junk DNA, might play important roles in affecting the stability of chromosomes and in regulating nearby genes. . . . **ROSWELL PARK CANCER INSTITUTE** received a five-year, $2 million grant from the National Institute of Allergy and Infectious Diseases to examine mechanisms of acute inflammation. **Brahm Segal**, chief of infectious diseases, is the principal investigator. Segal and colleagues from Vanderbilt University Medical Center will analyze NADPH oxidase, an enzyme complex that helps defend against infections. The study will also offer new insights into chronic granulomatous disease, a rare inherited disorder of the NADPH oxidase. . . . **CITY OF HOPE** research nurses **Marcia Grant** and **Rose Virani** will be honored by the Oncology Nursing Society at the society's annual Congress next month. Grant, professor in the Department of Population Sciences, was selected for the Lifetime Achievement Award, and Virani, senior research specialist, will receive The Pearl Moore Making a Difference Award. Also at City of Hope, **Rahul Jandial** was named section head of the spine program in the Division of Neurosurgery. He manages the neurological treatment of brain and spine cancers, focusing on the removal of tumors along the spine and reconstruction of the affected area. Jandial will also conduct research into neural stem cells and their role as possible origins of brain tumors. Jandial was chief resident neurosurgeon at University of California, San Diego, Medical Center. He was a clinical instructor for the Department of Neurological Surgery at the University of California, San Francisco, and an adjunct professor in the Scripps Research Institute. Also, Jandial provided health education to the general public as a health and science correspondent for the ABC affiliate in San Diego, and as a regular health contributor to the Orange County Register. . . . **JASON WEBER**, associate professor of medicine in the Division of Oncology at Washington University School of Medicine in St. Louis, received at $4 million Era of Hope Scholar Award from the Department of Defense. Weber will study potential new ways to control breast cancer cell growth. Surprisingly, that's an area of research that has been relatively neglected, he said. "For the last two decades, much of cancer research has focused on how to prevent cancer cells from dividing," says Weber, also associate professor of cell biology and physiology and a researcher with the Siteman Cancer Center at Barnes-Jewish Hospital and Washington University. "But before cancer cells divide, they have to grow larger. My lab is investigating molecular processes that control cell growth. We think that we can find ways to interfere with growth processes. And once you stop cancer cells from growing, it should be easier to kill them." Era of Hope Scholar Awards are given by the DOD to individuals in the early stage of their careers who have shown a high potential for innovation in breast cancer research. Three or four of the five-year awards are given each year.

Funding Opportunities:

NIH Challenge Grants

RFA-0D-09-003: Recovery Act Limited Competition: NIH Challenge Grants in Health and Science Research (RC1).

Application Due Date: April 27.

NIH has received new funds for Fiscal Years 2009 and 2010 as part of the American Recovery and Reinvestment Act of 2009. NIH has designated at least $200 million for a new initiative called the NIH Challenge Grants in Health and Science Research, http://grants.nih.gov/grants/funding/challenge_award/.

This new program will support research on topic areas which address specific scientific and health research challenges in biomedical and behavioral research that would benefit from significant 2-year jumpstart funds. NIH Institute and Centers have selected specific Challenge Topics within each of the Challenge Areas. The research in these Challenge Areas should have a high impact in biomedical or behavioral science and/or public health.

As part of the Recovery Act, the NIH invites, through this limited competition, NIH Challenge Grant (RC1) applications from domestic institutions/organizations proposing novel research in areas that address specific knowledge gaps, scientific opportunities, new technologies, data generation, or research methods that would benefit from an influx of funds to quickly advance the area in significant ways. This program is designed to support research in scientific areas identified by the Institutes and Centers.

This FOA will utilize the NIH Challenge Grant (RC1) award mechanism.

Funds Available and Anticipated Number of Awards. This initiative is funded under the Recovery Act. NIH has designated at least $200 million in FYs 2009 - 2010 to fund 200 or more grants, contingent upon the submission of a sufficient number of scientifically meritorious applications. In addition, Recovery Act funds allocated to NIH specifically for comparative effectiveness research may be available to support additional grants. Projects receiving these funds will need to meet this definition of CER: "a rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients. Such a study may compare similar treatments, such as competing drugs, or it may analyze very different approaches, such as surgery and drug therapy." Such research may include the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data as they apply to CER.

Budget and Project Period. Budget requests should be commensurate with project needs up to a two-year project period. The requested budget may not exceed $500,000 total costs per year for a maximum of $1,000,000 total costs over a two-year project period.

Other NIH Opportunities

RFA-CA-09-011: The Integrative Cancer Biology Program: Centers for Cancer Systems Biology. http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-09-011.html

PA-09-110: Career Enhancement Award for Stem Cell Research (K18). http://grants.nih.gov/grants/guide/pa-files/PA-09-110.html

PA-09-113: Manufacturing Processes of Medical, Dental, and Biological Technologies (SBIR R43/R44). http://grants.nih.gov/grants/guide/pa-files/PA-09-113.html

PA-09-114: Manufacturing Processes of Medical, Dental, and Biological Technologies (STTR R41/R42). http://grants.nih.gov/grants/guide/pa-files/PA-09-114.html

SGO, ACOG Breast Cancer Fellowship Program

The Society of Gynecologic Oncologists and the American College of Obstetricians and Gynecologists have developed a breast disease fellowship training program for gynecologic oncologists.

Supported by a grant of $75,000 from ACOG, the program provides support for a gynecologic oncologist to complete a one-year fellowship training in the care and treatment of breast cancer and related disease.

Applications will be accepted beginning this summer for the one-year fellowship, slated to begin in 2010. The process calls for both the prospective gynecologic oncology fellow and his/her institution to jointly submit an application.

The program was designed to be flexible in nature, allowing the fellowship to be offered at a different institution each year, and afford a greater number of gynecologic oncology fellows interested in advanced training in breast disease the opportunity to apply, regardless of their current location.

Further information and application materials will be available at www.acog.org and www.sgo.org.

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. 24 No. 2
February 2009

Business & Regulatory Report

Oncology Management

US Oncology Earnings Down $370 Million, Company Cites ESA Safety Concerns

US Oncology lost $370.5 million for the year ended Dec. 31. This represents a decrease of $377.7 million compared to 2007, when net income was $7.2 million.

The company said its reductions on earnings from erythropoiesis-stimulating agents for the year added up to $26 million. However, most of the decline in net income was attributed to a $380 million "impairment of goodwill" charge the company took during the first quarter.

According to the company, the charge reflected "reduced dependencies on the medical oncology segment and the impact of safety concerns about

(Continued to page 2)

Clinical Trials

Amgen, Takeda Resume Enrollment In Phase III MONET1 Trial For NSCLC

Amgen (NASDAQ: AMGN), **Millennium: The Takeda Oncology Company**, and its parent company **Takeda Pharmaceutical Company Limited** said the independent data monitoring committee for the MONET1 trial has recommended the trial resume enrollment of patients with non-squamous non-small cell lung cancer.

The decision follows a three-month enrollment suspension.

MONET1 is a phase III study evaluating motesanib (AMG 706) in combination with paclitaxel and carboplatin for the first-line treatment of advanced NSCLC. Motesanib is being co-developed by Amgen, Millennium and Takeda.

The recent DMC guidance recommends the trial be reopened only to patients with non-squamous cell histology. Non-squamous cell NSCLC is a histological subtype of NSCLC representing approximately two-thirds of the study population. Amgen, Millennium and Takeda plan to follow this recommendation, which will require modifications to the study design of MONET1. Enrollment will resume once these changes are sanctioned by appropriate global health authorities, the companies said.

Last November, the DMC recommended treatment discontinuation in subjects with squamous histology, and enrollment suspension in subjects with non-squamous histology.

This recommendation was based on an observation of higher early mortality rates in the motesanib group, compared to the placebo group.

(Continued to page 4)

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

US Oncology Takes Charges Due To ESA Restrictions

(Continued from page 1)

ESAs." Last year, FDA restricted labeled indications for ESAs, and the Centers for Medicare and Medicaid Services issued a National Coverage Decision limiting their use.

Full impact of restrictions remains unknown as FDA is yet to approve a Risk Evaluation and Mitigation Strategy for the agents. The sponsors of ESAs—Amgen Inc. and Hohnson & Johnson, filed their REMS proposals with FDA last August, but the agency hasn't yet implemented these strategies.

"We believe a possible impact of REMS could be further reductions in ESA utilization," US Oncology said in a statement. The company said it expects that REMS would be released during the first quarter of 2009.

Excluding the impairment of goodwill charges, the company's adjusted Earnings Before Income Taxes, Depreciation and Amortization were at $219.6 million, a $700,000 increase from 2007.

"We continue to transform the organization from a practice management company to a national cancer care platform with deep clinical capabilities," Bruce Broussard, president and CEO, said in a statement. "The strengthening of our clinical capabilities coupled with pressures on medical oncology practices is increasing our development success, contributing to our overall patient growth of ten percent."

THE CANCER LETTER

To subscribe, visit www.cancerletter.com

Business & Regulatory Report
Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg

Editorial: 202-362-1809 Fax: 202-379-1787
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. ISSN 1053-9611.

Cancer Clinics of Excellence, LLC, of Scottsdal, Ariz., announced the completion of its 62nd comprehensive Evidence-Based Treatment Protocol covering 11 of the leading oncology disease states.

"Our 200+ member national oncology group is now fully prepared to launch the protocols across its network in 16 States," announced Frederick Schnell, of Central Georgia Cancer Care, Macon, Ga., and CCE's Chief Clinical Officer.

Collexis Holdings Inc. (BULLETIN BOARD: CLXS) of Columbia, S.C., said the **American Association for Cancer Research** has licensed the Collexis' Reviewer Finder and Journal Dashboard applications for the six AACR cancer research journals.

"The Collexis Review Finder application will certainly enhance and improve our peer review process as we continuously strive to target the most appropriate reviewers", stated Diane Scott-Lichter, Publisher of AACR. "The Journal Dashboard will provide us with key insights concerning the positioning of our journals in the area of cancer research."

The Reviewer Finder helps assists in reducing the time to identify the most qualified reviewers from hours to virtually minutes by automatically suggesting best matching reviewers for a manuscript and identifies potential conflicts of reviewers based on co-authorship and institutional affiliation.

Impac Software of Sunnyvale, Calif., part of the Elekta Group, announced its collaboration with the **National Comprehensive Cancer Network** to license NCCN's clinical care content to clinicians utilizing MOSAIQ, Impac's oncology electronic medical record.

MOSAIQ will be the first oncology EMR to embed an intelligent search engine that dynamically links to the NCCN Clinical Practice Guidelines in Oncology. The NCCN Guidelines are used by clinicians to shape care recommendations covering 97% of all patients with cancer and are updated on a continual basis.

The NCCN guidelines, developed through an explicit review of evidence and recommendations from medical experts, address cancer detection, prevention and risk reduction, workup and diagnosis and treatment and supportive care.

In addition, MOSAIQ also will provide active access to the NCCN Drugs & Biologics Compendium, which delineates uses of drugs and biologics in the care of patients with cancer, listing FDA-approved disease

indications as well as off-label recommendations for use, and to the NCCN Chemotherapy Order Templates.

"Simplified, real-time access to NCCN's evidence-based clinical content is expected to enhance the delivery of standardized care and improve patient safety," said Joel Goldwein, vice president, medical affairs, for the Elekta Group. "Many of Impac's customers are NCCN member institutions. However, simplifying access to NCCN's clinical content will significantly increase the use of NCCN Guidelines throughout Impac Software's existing customer base, and in hundreds of cancer care centers."

In a related development, NCCN announces updates to the guidelines for breast cancer and breast cancer risk reduction.

Diagnostic additions include a recommendation for genetic counseling if the patient is high risk for hereditary breast cancer, as well as six new recommendations detailing when MRIs may be helpful in breast cancer evaluations.

Conversely, the updated breast cancer guidelines state that PET/CT scanning is not recommended for evaluation of newly diagnosed patients with early stage disease except in those clinical situations where other staging studies are equivocal or suspicious, and even in these situations that biopsy is recommended.

The NCCN guideline panel members for breast cancer note that although there is limited evidence demonstrating the utility of PET/CT scan in the staging of patients, they consider biopsy to be more likely to provide useful staging information.

The updated NCCN guidelines continue to recognize bisphosphonates as the preferred intervention to treat osteoporosis in women with breast cancer, while the use of estrogen, progesterone, or selective estrogen receptor modulators is discouraged.

Significant additions were made to the portion of the NCCN guidelines providing recommendations for patients undergoing breast reconstruction following surgery.

It is now recommended that women receive an evaluation detailing the likely cosmetic outcome of a lumpectomy prior to the actual surgery. Furthermore, women who are not satisfied with the cosmetic outcome following completion of breast cancer treatment should be offered a plastic surgery consultation.

Notable additions to the NCCN guidelines for breast cancer risk reduction include updates to two risk-reduction agents, tamoxifen (Soltamox, AstraZeneca) and raloxifine (Evista, Eli Lilly and Company).

Tamoxifen is recommended for premenopausal women with a history of atypical hyperplasia to reduce breast cancer risk. For postmenopausal women, raloxifene is listed as equivalent to tamoxifen in reducing the risk of developing invasive breast cancer; however, it did not provide the same level of risk reduction for developing non-invasive breast cancer.

Nucletron and **Advanced Radiation Therapy** announced an exclusive global, strategic partnership to offer the AccuBoost system with the microSelectron high-dose rate brachytherapy afterloader for the treatment of breast cancer.

The partnership will enable clinicians to deliver boost brachytherapy as part of the whole breast irradiation procedure, providing a superior treatment option with the ultimate goal of improving clinical outcome.

The partnership allows radiation oncology centers to implement ART's innovative technology in image-guided HDR breast brachytherapy on a pay-per-patient pricing model, along with a full complement of Nucletron's treatment planning, treatment delivery, training, licensing, reimbursement, and customized service support.

ART's expansion of AccuBoost technology through its global partnership with Nucletron is intended to reduce the barriers to adoption of brachytherapy for cancer centers previously deterred by the initial start-up costs usually associated with implementing a breast brachytherapy program.

Silicon Graphics, Inc. (NASDAQ: SGIC) of Sunnyvale, Calif., said it will provide the high-productivity solutions for the UK **Institute of Cancer Research**.

Silicon Graphics was selected to equip, over the next five s, an initiative in integrated network biology at London-based ICR. Expected to open in spring 2009, the initiative in integrated network biology at The Institute will use the Silicon Graphics compute, storage and visualization solutions.

The institute's effort aims to study how networks of cancer cells interact with each other and surrounding tissues to metastasize or spread throughout the body.

"Studying the dynamics of cellular networks will put unprecedented demands on our technology infrastructure, generating enormous data sets that must be processed rapidly, visualized interactively, and accessed on the fly," said Rune Linding, head of the Cellular and Molecular Logic Team at The Institute of Cancer Research.

A report by the **Institute of Medicine** provides further evidence of importance of health insurance.

The study suggests that when local rates of uninsurance are relatively high, even people with insurance are more likely to have difficulty obtaining needed care and to be less satisfied with the care they receive.

In 2007, nearly one in 10 American children and one in five non-elderly adults had no health insurance. The average amount employees paid per year for family coverage in an employer-sponsored plan rose from $1,543 in 1999 to $3,354 in 2008. If there is no intervention, the decline in health insurance coverage will continue, concluded the committee that wrote the report.

The committee called on the president and Congress to begin efforts immediately to achieve health coverage for all Americans. Steps must be taken to reduce the costs of care and the rate at which health care spending is rising to make that coverage sustainable for everyone, the report adds.

"Policymakers and the public can no longer presume that those without health insurance are getting the care they need through safety-net services such as charity care and emergency departments," committee chair Lawrence Lewin, an executive consultant in health care policy and management, said in a statement. "The evidence clearly shows that lack of health insurance is hazardous to one's health, and the situation is getting worse because of the erosion of employment-based health coverage due to the current economic crisis. The nation must act now to solve the uninsurance problem."

The report responds to questions being raised in the national debate about health care reform, including whether having insurance is essential for gaining access to necessary services given the availability of charity and free emergency care, and whether lack of coverage has wider ripple effects on whole communities.

A significant amount of new evidence about the health consequences for individuals--particularly from comparisons of participants' health before and after they enrolled in Medicare, Medicaid, and the State Children's Health Insurance Program--has emerged since the IOM last studied the consequences of uninsurance in 2004. In addition, new research suggests that that high rates of uninsurance in communities can have spillover effects on the insured.

With health insurance, children are more likely to gain access to a regular source of care, immunizations and checkups, needed medications, asthma treatment, and basic dental services. Serious childhood health problems are more likely to be identified early, and those with special needs are more likely to have access to specialists. Insured children experience fewer hospitalizations and improved asthma outcomes, and they miss fewer days of school.

Adults without health insurance are much less likely to receive clinical preventive services that can reduce unnecessary illness and premature death. Chronically ill, uninsured adults delay or forgo checkups and therapies, including medications. They are more likely to be diagnosed with later-stage cancers that could have been detected earlier, and to die when hospitalized for trauma or other serious conditions, such as heart attack or stroke. Uninsured men and women with cancer, heart disease, serious injury, stroke, respiratory failure, pulmonary illness, hip fracture, and seizures are also more likely to suffer poorer outcomes, greater limitations in quality of life, and premature death. New evidence demonstrates that obtaining coverage lessens or reverses many of these harmful effects.

Based on the available evidence, the committee concluded that when a community has a high rate of uninsurance, the financial impact on health care providers may be large enough to affect the availability, quality, and cost of local services for everyone, even people who have insurance.

Additional information on the report can be found at http://iom.edu/americasuninsuredcrisis.

Clinical Trials:

Phase III Trial Of Motesanib Reopens To Patient Enrollment

(Continued from page 1)

A higher incidence of hemoptysis in the squamous population was also observed, the company said. Patients with non-squamous NSCLC receiving motesanib were allowed to continue treatment during the temporary suspension.

"This decision gives us confidence we have selected the right patient population to explore the clinical potential of motesanib in non-small cell lung cancer," Roger Perlmutter, executive vice president of research and development at Amgen said in a statement.

MONET1 (Motesanib NSCLC Efficacy and Tolerability Study) Trial has the primary endpoint of overall survival. Secondary endpoints include progression-free survival, objective response rate in patients with measurable disease, duration of response

and safety. Patients were randomized 1:1 to receive paclitaxel and carboplatin administered every three weeks with or without 125 mg motesanib taken daily.

Motesanib is a selective, oral agent that is being evaluated for its ability to inhibit angiogenesis by targeting vascular endothelial growth factor receptors 1, 2 and 3 (VEGFR1-3), the companies said. It is also under investigation for its potential direct anti-tumor activity by targeting a family of proteins called tyrosine kinases, including platelet-derived growth factor receptor (PDGFR), and stem cell factor receptor (c-kit), two proteins involved in cell proliferation.

ADVENTRX Pharmaceuticals Inc. (NYSE Alternext US: ANX) of San Diego said it has completed patient enrollment in its bioequivalence study of ANX-514 (docetaxel emulsion for injection).

ANX-514 is a reformulation of the chemotherapeutic agent Taxotere (docetaxel). In 2007, the aggregate worldwide market for Taxotere was in excess of $3 billion.

The study is a multi-center, open-label, randomized two-period crossover comparison of ANX-514 and Taxotere, with a primary endpoint of pharmacokinetic equivalence of ANX-514 and Taxotere and a goal of 28 evaluable patients.

The safety of a single dose of ANX-514 is being evaluated as a secondary endpoint. FDA has indicated that this single study, should it demonstrate bioequivalence between ANX-514 and Taxotere, would provide sufficient human data to support the submission of an NDA, the company said.

ANX-514 is a nano-emulsion formulation of Taxotere. ANX-514 is formulated without polysorbate 80 or other detergents and is intended to reduce the severity and incidence of hypersensitivity reactions, the compoany said.

Algeta ASA (OSE: ALGETA) said it's enrolling U.S. patients into the ALSYMPCA phase III trial evaluating Alpharadin for bone metastases in patients with hormone-refractory prostate cancer.

This decision follows an end-of-phase II meeting with FDA. Algeta began enrolling patients for its global phase III ALSYMPCA (ALpharadin in SYMptomatic Prostate CAncer) study in June 2008 and aims to enroll approximately 750 HRPC patients with bone metastases. Recruitment of US patients into the study is planned to commence this year, the company said.

The company said Alpharadin (radium-223) has demonstrated in phase II studies that it may prolong survival times, improves quality of life and offers a placebo-like safety profile.

The ALSYMPCA study is a double-blind, randomized, controlled trial that enrolls symptomatic HRPC patients who will be randomized to receive Alpharadin plus best standard of care or placebo plus best standard of care, the company said.

The primary efficacy endpoint of the trial is overall survival. Patients are being randomized 2-to-1 in favor of Alpharadin, which will be given as six injections of 50 kBq/kg body weight, four weeks apart. Secondary endpoints include time to occurrence of specified disease-related events, and time to progression of certain key biomarkers indicative of disease status, including blood levels of serum prostate-specific antigen and total alkaline phosphatase. The trial will monitor and evaluate both the acute and long-term safety profiles of Alpharadin treatment and its impact on quality of life, the company said.

Nektar Therapeutics (NASDAQ: NKTR) of San Carlos, Calif., said that the first patients have been dosed in a phase I dose-escalation study of NKTR-105, a PEGylated form of docetaxel.

The phase I study will assess the safety, pharmacokinetics and anti-tumor activity of NKTR-105 in about 30 patients with refractory solid tumors.

NKTR-105 is a form of docetaxel developed using Nektar's polymer conjugate technology, the company said.

Oncolytics such as docetaxel typically have sub-optimal half-lives which can limit their therapeutic efficacy, or have a safety and tolerability profile that limits their use, the company said. Nektar's polymer conjugate technology can be used to optimize the bioactivity of these drugs and increase the sustained exposure of active drug to tumor cells in the body.

Morphotek Inc., of Exton, Penn., a subsidiary of Eisai Corporation of North America, said it has commenced a multi-centered phase II study of its MORAb-009 monoclonal antibody in mesothelioma.

The study will evaluate MORAb-009, plus the chemotherapy drugs pemetrexed and cisplatinum, as a first-line treatment for patients with mesothelioma.

The primary objective of the study is to assess the efficacy of MORAb-009 as combination therapy with the current standard of care as determined by progression-free survival in patients with locally advanced malignant pleural mesothelioma.

Secondary objectives include safety and anti-

tumor activity of MORAb-009 as determined by objective response rate. The patient population includes individuals with locally advanced malignant pleural mesothelioma who have not received any prior treatment for their disease.

Morphotek said it expects to enroll up to 86 patients in the study, which is being conducted at clinical centers globally.

MORAb-009 is a monoclonal antibody that blocks the function of mesothelin, a cell surface protein on mesothelioma, pancreatic and a subset of other types of tumor cells that can allow these cells to attach, metastasize and grow, the company said. Mesothelin has been demonstrated by several independent studies to be expressed on virtually all mesothelioma tumors. Preclinical data support the theory that MORAb-009 achieves its pharmacological effect by two mechanisms: first, by blocking mesothelin's ability to interact with its target and second, by stimulating the patient's immune system to attack the tumor by specifically destroying those cells bound by MORAb-009.

The company said phase II clinical trial is supported by safety data and clinical observations from a recently completed phase I trial of MORAb-009 in patients with mesothelin-bearing tumors, including pancreatic, mesothelioma and ovarian cancers as well as data derived from preclinical models.

Drug Approvals & Applications:

Amgen Seeks FDA Approval For Denosumab In Bone Loss, And Osteoporosis Prevention

Amgen Inc. (NASDAQ: AMGN) said FDA has accepted its submission and filed a Biologics License Application for denosumab, an investigational RANK Ligand inhibitor.

Amgen is seeking approval of the agent for two indications: treatment and prevention of postmenopausal osteoporosis in women and treatment and prevention of bone loss in patients undergoing hormone ablation therapy for either prostate or breast cancer.

The Prescription Drug User Fee Act action date on the application is Oct. 19. Due to the interdependency of the data across the indications from more than 11,000 patients, both files will be reviewed simultaneously, the company said.

Amgen has also submitted marketing applications for use of denosumab for these indications in the European Union, Canada, Switzerland, and Australia.

Denosumab is the first fully human monoclonal antibody in late stage clinical development that specifically targets RANK Ligand, an essential regulator of osteoclasts, the company said.

Denosumab is being studied in a range of bone loss conditions including PMO and bone loss in patients undergoing hormone ablation for prostate and breast cancer, as well as for its potential to delay bone metastases and inhibit and treat bone destruction across many stages of cancer. Denosumab is also being investigated in rheumatoid arthritis.

GlaxoSmithKline and **Genmab A/S** (OMX: GEN) announced the submission of a Biologics License Application to FDA for Arzerra (ofatumumab) for refractory chronic lymphocytic leukemia.

If approved, ofatumumab would be the first anti-CD20 monoclonal antibody available for this patient population.

"The submission of the BLA for ofatumumab brings us closer to the possibility of providing a new treatment to patients with refractory CLL," said Lisa Drakeman, Chief Executive Officer of Genmab. "This is the first BLA ever filed for an antibody produced by Genmab and is a significant achievement in our partnership with GSK."

The submission is based on an analysis that included 138 patients with CLL who showed limited or no response to both fludarabine and alemtuzumab treatment (fludarabine alemtuzumab refractory) and patients who were refractory to fludarabine and considered inappropriate candidates for alemtuzumab due to bulky tumor masses (>5 cm) in their lymph nodes (bulky fludarabine refractory).

The primary endpoint of the study was assessment of response. The overall response rate seen in these patient groups treated with single-agent ofatumumab was 58% for the fludarabine alemtuzumab refractory group (n=59) and 47% for the bulky fludarabine refractory group (n=79).

The most common adverse events seen with ofatumumab were related to infusion reactions and infections. AEs seen in at least 10% of patients included fever, cough, diarrhea, rash, low white blood cell counts, fatigue, pneumonia, anemia, shortness of breath and nausea.

In clinical trials, infusion reactions that were serious yet manageable were seen in 3% of patients. One case of progressive multifocal leukoencephalopathy, a brain infection resulting in death or causing severe disability, and one case of tumor lysis syndrome were reported.

The companies also announced the initiation of an additional phase III study of ofatumumab in combination with fludarabine and cyclophosphamide for patients with CLL when initial treatment no longer works (second-line treatment).

The open-label study will randomize 352 patients to evaluate progression-free survival (PFS) of ofatumumab in combination with FC therapy versus FC therapy alone for the treatment of relapsed CLL. Enrollment for this study will begin shortly.

GSK and Genmab will conduct additional studies of ofatumumab in CLL and non-Hodgkin's lymphoma settings. In CLL, a phase III front-line study is evaluating ofatumumab combined with chlorambucil in patients with previously untreated CLL. In NHL, an ongoing phase II study will assess ofatumumab in patients with Waldenstrom's Macroglobulinemia - a rare type of slow-growing NHL.

Finally, a phase II study is evaluating ofatumumab plus ICE or DHAP chemotherapy regimen in relapsed/refractory diffuse large B-cell lymphoma.

Ofatumumab is a monoclonal antibody that targets a membrane-proximal small loop epitope on the CD20 molecule on B-cells.

GTx, Inc. (NASDAQ: GTXI) said FDA has accepted for filing and review the New Drug Application for toremifene, an oral selective estrogen receptor modulator, which GTx seeks to market for the prevention of bone fractures in men with prostate cancer on androgen deprivation therapy.

The NDA is supported by results from a two-year, double blind, placebo controlled, randomized phase III clinical trial of 1,382 men with advanced prostate cancer on ADT, the company said.

Tigris Pharmaceuticals Inc. of Bonita Springs, Fla., said its Investigational New Drug application for geranylgeranyltransferase inhibitor (GGTI-2418) has been accepted by FDA.

This will allow the company to open a phase I study evaluating GGTI-2418 during the first quarter of 2009. GGTI-2418 is a synthetic peptidomimetic inhibitor of geranylgeranyltransferase I (GGTase I) that induces apoptosis by downregulating several pivotal oncogenic and tumor survival pathways.

Tigris licensed the exclusive worldwide rights to GGTI-2418 from Yale University and the University of South Florida.

GGTI-2418 is a synthetic peptidomimetic inhibitor of GGTase I that appears to induce apoptosis by downregulating several pivotal oncogenic and tumor survival pathways, the company said. GGTase I catalyzes the lipid posttranslational modification which is required for the function of Rho GTPases. GGTase I inhibitors block Rho function in cancer cells and induce a G1 phase cell cycle arrest by a mechanism involving induction of the CDK inhibitors p21waf and p27kip, CDK2 and CDK4 inhibition and hypophoshorylation of the tumor suppressor Rb.

Tigris is a privately held company.

Cellectar Inc., of Madison, Wisc., said FDA has cleared its Investigational New Drug application for its (131)I-CLR1404 drug candidate for testing in advanced solid malignancies.

The first phase I study will enroll up to 9 patients and will include drug dosimetry calculations and biodistribution assessments. The second phase I study will be a dose escalation study evaluating the Maximum Tolerated Dose of (131)I-CLR1404 in patients with advanced solid malignancies. Both studies will be performed at four U.S. medical centers.

(131)I-CLR1404 is a small-molecule, phospholipid ether analog that combines lipid-like properties with a cancer therapeutic beta-emitting radioisotope. Preclinical animal studies demonstrated that (131)I-CLR1404 significantly slowed the growth of malignant solid tumors and resulted in improved survival, the company said. Cellectar is a privately held company.

Deals And Collaborations:

Cell Therapeutics Sells Interest In Zevalin Joint Venture

Cell Therapeutics Inc. (NASDAQ and MTA: CTIC) said it has exercised its option to sell its 50% ownership interest in the Zevalin joint venture to **Spectrum Pharmaceuticals Inc.** for $18 million.

CTI and Spectrum established a joint venture in December 2008 to develop and commercialize Zevalin. At that time CTI contributed all of the Zevalin related assets to the joint venture and sold to Spectrum a 50% membership interest in the joint venture for $15 million plus milestone payments.

CTI said it will focus its resources on the approval of pixantrone for relapsed aggressive non-Hodgkin's lymphoma and OPAXIO for non-small cell lung and ovarian cancer. CTI estimates that as a result of the sale of the Zevalin interest, it will reduce expenses by approximately $15 million annually from activities previously associated with Zevalin while providing CTI

with non-dilutive source of operating capital.

"CTI continues to believe in the value of Zevalin as a commercially attractive product and effective form of cancer therapy; however, with the impressive clinical trial results for pixantrone and given the company's need for operating capital, we are compelled to exercise our option and focus our resources on pixantrone," said James Bianco, CEO of CTI.

"CTI has been proud to have provided Zevalin to patients since we acquired it in December, 2007 and having the foresight to bring the first line consolidation for indolent NHL data to the FDA for potential label expansion in the front line consolidation setting. With the progress we made in removing many of the barriers that prevent its more widespread use, we are confident Spectrum will be able to ultimately make Zevalin a commercially attractive product."

At the closing of the sale of CTI's 50% membership interest in the joint venture to Spectrum, CTI will receive $6 million, with the remainder of the $18 million to be paid within 90 days following such closing. The closing of the sale option transaction is contingent upon the satisfaction of certain closing conditions, including the delivery of a legal opinion from counsel to CTI, as specified in the operating agreement for the Zevalin joint venture. CTI believes that it will be in a position to promptly satisfy all of the closing conditions.

Agendia, of Huntington Beach, Calif., said its breast cancer test MammaPrint will be offered as standard of care for all eligible early stage breast cancer patients at the **Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital** (NKI-AVL).

The NKI-AVL said MammaPrint provides better guidance for decisions regarding adjuvant therapy. As one of the participating centers in the MINDACT trial NKI-AVL is offering MammaPrint to patients. In future, however, NKI-AVL will also make MammaPrint available to patients who fall outside MINDACT's inclusion criteria.

Oncolytics Biotech Inc. (TSX:ONC, NASDAQ: ONCY) of Calgary and the **Cancer Therapy & Research Center** at The University of Texas Health Science Center in San Antonio, announced a broad preclinical and clinical collaboration involving up to five, open-label, phase II studies exploring the use of REOLYSIN in combination with chemotherapy for various cancer indications.

These indications are expected to include melanoma, pancreatic cancer, squamous cell lung, liver and K-RAS mutated colorectal cancers in combination with standard chemotherapeutics, the company said. This research program is in addition to phase II trials in sarcoma and refractory head & neck cancers, sponsored by Oncolytics that are currently underway at this site.

PDS Biotechnology of Indianapolis said it has obtained an exclusive license from German-based **Merck Eprova AG** to utilize Merck Eprova's proprietary chiral lipid DOTAP Chloride in Versamune-HPV and other products in development based on the Versamune technology.

The use of enantiomerically pure DOTAP Chloride shows enhanced adjuvant activity compared to the racemate, the companies said. Merck Eprova AG will be providing enantiomerically pure DOTAP Chloride manufactured under cGMP for use in clinical and commercial drug products developed with PDS Biotechnology's Versamune nanoparticle technology.

PDS Biotechnology will own the intellectual property rights to products incorporating the chiral DOTAP lipids for immunotherapeutic applications.

Versamune-HPV is an immunotherapy drug which has demonstrated promise in curing HPV infection and HPV-related cancer in preclinical animal and human model studies, the company said.

Based on promising in vivo and in vitro efficacy data, PDS Biotechnology has been awarded grants by the US National Institutes of Health/National Cancer Institute to develop Versamune-HPV and Versamune-Melanoma. Versamune-Melanoma is being developed to treat melanoma.

Cephalon Inc. (NASDAQ: CEPH) of Frazer, Penn., said its wholly-owned subsidiary, Cephalon International Holdings Inc., intends to make a takeover offer for Arana Therapeutics Limited.

Arana has a pipeline of biologic compounds for inflammatory diseases and cancer at various stages of discovery and development. The offer has the support of the Arana independent directors and will be recommended to Arana shareholders in the absence of a superior proposal, Cephalon said.

Arana is a biopharmaceutical company focused on developing antibody-based drugs. The company's lead compound, ART621, is a new generation tumor necrosis factoralpha blocker in development for inflammatory diseases. Arana has a strong patent portfolio related to anti-TNF alpha antibodies and receives royalties from Abbott Laboratories and Johnson & Johnson, the makers of HUMIRA and REMICADE, respectively.