THE CANCER LETTER

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Advisors Say 10% Payline "Not Tenable," All NCI Programs Must Share Budget Cuts

By Kirsten Boyd Goldberg

In an attempt to limit further drop of the payline for investigator-initiated grants, external advisors to NCI have called for a comprehensive review of large research programs, including those that define Andrew von Eschenbach's legacy as institute director.

The chairmen of three NCI advisory boards said in a joint meeting earlier this month that a review is needed to balance reductions in Research Project Grants.

Earlier this year, NCI announced budget cuts of up to 29 percent for

(Continued to page 2)

In Brief:

Lance Armstrong Foundation Forms Collaboration With NCI Cancer Centers

LANCE ARMSTRONG FOUNDATION formed the LIVESTRONG Survivorship Center of Excellence Network, a partnership among the LAF, NCI-designated comprehensive cancer centers, and community affiliates. Network members include UCLA Jonsson Comprehensive Cancer Center, Fred Hutchinson Cancer Research Center, University of Colorado Cancer Center, Memorial Sloan-Kettering Cancer Center, and Dana-Farber Cancer Institute. "Extended cancer survival is a relatively new phenomenon, so the current pace of research and of the development of effective models of care lags behind the need," said **Caroline Huffman**, LAF survivorship network officer. The network will serve as a source of information, care, and services for survivors. . . . **MULTIPLE MYELOMA Research Foundation** received the Best in America Seal of Excellence from Independent Charities of America, a nonprofit association. The seal is awarded to charities that document on an annual basis that they meet the highest standards of public accountability, program effectiveness, and cost effectiveness. MMRF also is four-star rated from Charity Navigator, A+ rated by the American Institute of Philanthropy, meets the Better Business Bureau's Wise Giving Alliance for Charitable Accountability, and is recognized by NCI for meeting stringent research review guidelines for funding research grants, said **Scott Santarella**, MMRF executive director. . . . **ASCO Foundation** received a $290,000 grant from the John A. Hartford Foundation for physicians pursuing academic careers in geriatric oncology. The new grant follows a 2001 grant from the Hartford Foundation that allowed ASCO to award 10 U.S. medical centers three-year grants to develop geriatric oncology

(Continued to page 8)

NCI Advisors: Big Programs Need To "Share The Pain"

(Continued from page 1)

funded RPGs and said it could fund only the top 11th percent of R01 investigator-initiated grants. This level of funding is "not tenable" in the long-term, the advisors said.

However, the President's funding proposal for FY 2007 would cut NCI's budget by $40 million, or 0.8 percent. NCI officials earlier this month said that if the President's budget is enacted, funding for competing Research Project Grants would be cut by $27 million, or 6.2 percent, from a total of $444 million in FY 2006. Non-competing grants would be cut by $21 million, or 1.3 percent, from the FY06 level of $1.664 billion.

Though NCI officials declined to project the impact of these cuts, observers said that it was clear that the payline is dipping into the single digits. Would the institute's largest programs—and von Eschenbach's controversial "strategic initiatives"—share the pain?

"There is a strong feeling on the part of the leaders of the external advisory groups that this provides us an opportunity to re-examine the whole NCI research portfolio," Robert Young, chairman of the NCI Board of Scientific Advisors and president of Fox Chase Cancer Center, said at a March 13 meeting. "Meritorious programs in good times may not all be sustainable in bad times. All of the major programs, in addition to investigator-initiated research, need review, and that review may result in either increases or decreases, or sunsetting the programs."

In a presentation at the annual joint meeting of the BSA and the Board of Scientific Counselors, Young listed several large programs costing $300 million to $400 million a year that he said should be reviewed. These include the NCI intramural research program, cancer centers and Specialized Programs of Research Excellence, drug development, and cooperative groups.

Young also listed new initiatives in nanotechnology, proteomics, and The Cancer Genome Atlas, as well as four large-scale contract programs each costing over $100 million a year—the Early Detection Research Network, the Spiral CT lung cancer screening trial, the NCI Alliance for Nanotechnology, and the NCI Chemoprevention Drug Development Program.

"In the present environment, nothing ought to be off the table in terms of taking a re-look," Young said.

In von Eschenbach's four years as NCI director, external advisors reviewed several large programs including the cancer centers, SPOREs, and the clinical trials program, which includes the cooperative groups. NCI implemented recommendations from the cancer centers and SPOREs review, and has begun implementing changes as a result of the clinical trials review.

Young said his comments were endorsed by Margaret Tempero, chairman of the BSC-Clinical Sciences and Epidemiology; Thea Tlsty, chairman of the BSC-Basic Research; and Franklyn Prendergast, chairman of the planning and budget subcommittee of the National Cancer Advisory Board.

The advisors offered to take part in a comprehensive examination of NCI programs. "The leadership of the NCAB, the BSA, and the two BSCs has expressed their willingness to assist the NCI leadership in any such review," Young said.

NCI officials didn't indicate willingness to accept such review.

The institute recently went through a process to cut 5 percent from division budgets, said John Niederhuber, NCI chief operating officer.

"We are trying our best to address our strategic priorities by funding new initiatives," Niederhuber said. "We do not want to hunker down. We do not want to be stagnant. It is our responsibility to continue initiatives that enable our investigators to be on the cutting edge of the science. Maintaining the number of competing awards is very important to us. We are doing everything possible to do that."

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NCI Director von Eschenbach said the institute has been doing what Young recommended, looking "at the entire portfolio," especially the "big-ticket items," and ensuring that the expenditures are justified.

"We have the largest number of cancer researchers today [and] we've funded the largest number of RPGs we've ever funded, so it's not that we're in bad shape," von Eschenbach said. "We're actually celebrating success, in that it's the greatest it's ever been. But the questions are, How do we maintain that momentum? How do we maintain that trajectory, recognizing that there is not simply an unlimited amount of dollars to allow that pool to continue to grow in an unlimited way?"

Nearly half of NCI's $4.8 billion budget funds RPGs, which include investigator-initiated grants, small business grants, and cancer center and SPORE grants.

"I don't think we can assume that the RPG pool is off the table, because it's not off the table at NIH," von Eschenbach said. "It's not off the table at Congress. They wouldn't know an RPG from a SPORE if it fell on them. The point is, they look at the numbers and they go, 'Hmm, all your dollars are in this pool.' They want to find out what's going on inside that pool. So, this pool is going to be subject to external scrutiny at a number of different levels."

Young: Review Would Ensure Balance

Young said his remarks reflected discussions at NCI's annual "joint boards retreat" last Jan. 10, where the institute sought advice on allocating its budget. That meeting wasn't open to the public.

"NCI did a very creative job of presenting a variety of budget scenarios and asked us to look at the impact of shrinking number of grants, shrinking size of grants, shrinking duration of grants, and gave us an idea of what the impact of those variations might be on the overall RPG pool," Young said to the BSA and BSCs at the March 13 meeting.

At the January budget retreat, the advisors didn't have time to discuss other issues that arose, including "how to evaluate the existing programs in a broad-spectrum manner, what kind of balance should one strive for between new initiatives and stabilizing the existing infrastructure that's been built as a result of the doubling [of the NIH budget], and the balance between extramural and intramural science," Young said.

However, the advisors made some recommendations about RPG funding, Young said. "This is, indeed, 'Sophie's Choice,'" he said. "It's not that everybody loves these conclusions. It is they believe these are the best conclusions one can make with the environment in which we exist."

—Stabilize grant numbers by reducing budgets awarded.

—Protect young investigators with preferential paylines.

—Pursue joint funding mechanisms with non-NIH partners.

—Limit the number of grants held by a single investigator.

"There is a very strong feeling in the external community of researchers that R01 grants at the 10th percentile—and I know the story about the number of people coming in, and blah, blah, blah—the 10th percentile is simply not tenable on a long-term basis," Young said.

Other NCI programs ought to "share the pain" with investigators, but across-the-board cuts aren't "an adequate solution," Young said. "It's very clear that some programs have already experienced a significant amount of reduction. Certainly, we are all too aware in the external community of the impact that's already been made in the investigator-initiated research environment with 11th percentile paylines, and 29 percent reduction in funded grants, and the disappearance of cost-of-living increases—which seems subtle except when you multiply it by five [years], it's not so subtle."

Young expressed frustration with the BSA's limited scope of reviewing NCI concepts for grant and contract programs. "It doesn't seem to make much sense to spend three months agonizing over an RFP or RFA for $7 million, when we're talking about the kinds of investments we're making in large-scale NCI programs," Young said.

An overall review would enable NCI and its advisors to make sure that research is balanced between basic, translational, and population science, Young said. Also, it could enhance communication between programs and communication with the public, he said.

"The cancer community and the public need to define what constitutes return on investment," Young said. "That's a term that's used frequently in these discussions, and it seems to imply a short-term result that exceeds the capacity of most of the history of science. We need to do a better job of trying to explain what we mean and what we can anticipate from return on investment in a basic science environment."

Intramural Program Doesn't Always Deliver

In a related presentation following Young's remarks, BSC Chairman Tempero, deputy director of the

University of California, San Francisco, Cancer Center, said the time is right for "some serious discussions about certain aspects" of NCI's four large programs.

Tempero warned that her remarks about the programs should not be considered "recommendations," but "ideas" that the board chairmen discussed:

—Intramural program: "The intramural program has about 50 percent more budget than the entire cancer centers and SPOREs. So the intramural program ought to be a centerpiece for us. Arguably, Thea and I have been advocates of the intramural program, but we are the first ones to admit—and I think the leadership of the NCI would admit, too—that the intramural program isn't always delivering what it should deliver. So how do we address that? Can we streamline, should we streamline the mission of the intramural program?

"What if the intramural program was the center for risk stratification and early detection? Could it leverage all of its resources into an area that is, arguably, underrepresented by our entire community?

The intramural program should develop strategic partnerships with extramural program, she said. "There's tremendous infrastructure at the NCI. How is that infrastructure being leveraged to help extramural programs that are going to have tighter and tighter constraints over how they function?"

The intramural program should be more involved in the Clinical Trials Working Group and the Translational Research Working Group, Tempero said. "I was kind of disappointed, I have to say, at the Translational Research Working Group [meeting] to see that the intramural program was really very poorly represented," she said.

Within the program, resources should be aligned with scientific strengths, she said. "We know from our reviews that the NCI leadership is trying to do this. Should they do it with an even more quicker, serious effort, looking at their centers of excellence?"

One possible area the program could emphasize is genetics. "We don't understand the true inventory of genetics within the NCI and how that interfaces with the rest of NIH," Tempero said. "Could it be possible to circle the wagons around some of these really important things that the intramural program at the NCI does better than virtually anyone else?"

—Cancer Centers: "Perhaps we need to re-look at our cancer center mechanism and redefine the criteria for success, permit more flexibility in our mission. Maybe centers can be a little bit different, and that's OK. We need to simplify the application and review processes. In a time when we have all these budget constraints, our cancer center leadership across the country are looking to do their own strategic partnerships to raise their own private sources of funding, and I have to say, it takes an entire year out of our planning process just to prepare for our application and defend our application.

"How do we facilitate value-added benefits from other NIH-funded resources? Right now the Clinical and Translational Science award program, which is trans-NIH program, is being competed. There are going to be a lot of resources in that that our cancer centers ought to be able to take advantage of. How can the NCI help leverage that and broker that for us so that we can benefit from that investment?

"The NCI really should be helping us in the centers broker strategic partnerships, not only with the intramural program, but with other centers and industry. Our contracts and grant mechanism is very cumbersome. It's hard to subcontract. We don't have mechanisms that really encourage consortia. It's very complicated business from an administrative point of view."

—Drug development: "I think we really, seriously, need to redefine the role of NCI and differentiate it from the role of industry, but at the same time, taking the industry approach, the business approach, to drug development with project teams, diagnostic applications, timely transportation to the appropriate consortium or cooperative groups."

—Cooperative groups: "We really need to minimize the redundancy and reward collaboration. This has to be done quickly. We are, right now, trying to support cooperative group activities which are a mandate at our cancer centers, and we're doing it with not enough dollars for accrual. We have to provide institutional sources of support, which we now are going to need for other purposes. If we can align the priorities and contract the activities to increase payments for accrual, we might be able to actually get something done."

Under the President's budget proposal, NCI would cut funding for the intramural program by about $3 million, or 0.5 percent of the program's $699 million budget, Niederhuber said. "We are developing the ability to optimally manage our research investments [in the intramural program]," he said. "We continue to refine this process in terms of being able to look at our portfolio and balance what we are actively supporting and doing against our resources and against what we see as future opportunities."

"We Have To Do Something About The Payline"

The proposed 6.2 percent cut to competing RPGs would be likely to once again lower the payline, NCI

advisors said.

"It's going to be hard to exist in a 10th percentile world," said BSA member Shelton Earp, director of the UNC Lineberger Comprehensive Cancer Center. "We have infrastructure at universities that… have been built up, in the same way the intramural program does. The major hit will be on new grants in the future. I think it speaks to what Bob and Margaret were saying, that we really do need to examine things across the board…. I do think we're going to have to do something about the payline."

The projected FY07 budget is "the beginning of a planning phase," Niederhuber replied. "Remember, too, that the RPG pool is the largest part of the budget, 45.3 percent of the overall NCI budget."

BSA member Richard Schilsky, chairman of the Cancer and Leukemia Group B, said the chairmen of the cooperative groups have begun to develop a variable reimbursement rate based on the complexity of a study.

"It's unlikely that the NCI budget is going to be able to sustain a two- to three-fold increase to the cooperative group budget line so that we can pay the cancer centers more money to involve patients in cooperative group trials," Schilsky said at the meeting. "We have to look for other sources of funding, and the logical partnership is with industry. The groups are fairly successful already in leveraging support from industry, but I think we need to do it in a way that we can assure deals with conflicts of interest and maintains the independent nature of cooperative group research, so that we're not somehow perceived as being an NCI-supported CRO for the pharmaceutical industry."

The group chairmen and NCI are planning a "retreat" in May to "brainstorm about how we can best leverage partnerships with industry and do it in a way that will continue to put resources into the system, but preserve the independent nature of cooperative group studies," Schilsky said.

BSA member Leroy Hood, president of the Institute for Systems Biology, said NCI awards for "big science" often are made to "groups that are not very good," but it's not clear whether the institute is able to deal with failures.

"I've seen some cancer centers that I've really wondered how they're getting funded still," Hood said. "The same is true of the new programs. You look at the nanotechnology centers. I think there are some superb ones, and maybe we ought to look at some of the others…. If we're going to try to free up funding for new programs, we have to bite the bullet and we have to decide we're going to get rid of programs that aren't performing. I guess the key question is, how do you do that, because there's so much ownership and so much political constituency and so forth? I guess I'm curious, Andy, as to how you see dealing with that issue?"

VON ESCHENBACH: "With patience and persistence. You're absolutely right. There are legacy programs. There are programs that built infrastructure. We faced this on a number of occasions, where resources like repositories or clinical trials are in place…. but the fact is, we couldn't just simply shut it down and wind up losing the investment.

"This portfolio is very much a real-estate portfolio, it's not a money market portfolio. You can't move and liquidate your assets that easily and that quickly. So you have to be much more strategic and much more longer-range. You have to be able to deal with the fallout that comes from something you disenfranchise, because there's always a constituency that sees that as a loss.

"We've shut down programs and we've dealt with the heat. I've taken it from a lot of different places, including on the Hill. When you explain it, and explain it well, and demonstrate that you had an open, transparent process in which to do it, eventually, it's viewed as a strategic business decision, not something that's capricious. Then you move on."

BSA member David Alberts said the program project grants (P01s) have been an effective way to establish a translational research program. "Yet, the program project grants are a real endangered species in the present climate," he said. "We need to understand the importance of those to the portfolio of the NCI and can't afford for them disappear, because they represent our best chance for really getting translational research from bench to bedside and having the impact we all want on cancer."

NIEDERHUBER: "I couldn't agree with you more. We are doing everything possible to maintain the program project instrument…. I've always been an extreme fan of the P01. We are doing everything we can to maintain that. A lot of our translation resides there. In many ways, the nanotechnology [program] is another way of doing a P01."

"What Can We Do?"

BSA member William Hait, director of the Cancer Institute of New Jersey, posed a fundamental question to the NCI leadership:

"What can we do as your boards to reverse the trend of shrinking allocations to NCI?" Hait asked at the March 13 meeting.

He received two different answers:

NIEDERHUBER: "I have a simple answer: If we could change some of the international events in the world, it would help a lot. I think there is a lot of pressure on this budget, on this Congress, a lot of demands. It's not anyone's fault. It's where we are. Some of us were at a panel meeting in Florida last week, and former Sen. Connie Mack said, you know, guys, you can forget about campaigning for increases, because this is the way it's going to be."

VON ESCHENBACH: 'There is a lot you can do. There is a huge amount. First of all, it starts with messaging. Suggesting that we cannot commit to using these resources in a way that can be demonstrated a direct benefit on the part of the American people because we're concerned that we might not live up to that commitment, we're frustrated, is the absolute—

"There is much better way. First of all, the ability to communicate to the public in every single opportunity that presents itself and other opportunities that we take advantage of and create—we all live in communities, we all have access to different forms of communication—to communicate the message that progress has been made, progress is being made, and what that investment is buying for them, and where that knowledge and that in terms of understanding cancer at its fundamental level, and where that is leading us in terms of solutions to the problem, has got to be told in a positive way that leads to expectations of hope. Not guarantees, not assurances. We're not talking about Pollyannaish promises.

"If anybody who has been doing this work for as long as the people in this room who doesn't feel the excitement, the enthusiasm, for what is coming by virtue of this incredible progress, you've got a problem.

"So I think messaging is important."

New NIH Office To Coordinate "Common Fund" For Research

By Kirsten Boyd Goldberg

NIH has established an Office of Portfolio Analysis and Strategic Initiatives to coordinate a "common fund" for research initiatives that would involve multiple NIH institutes and centers.

The new office was established in response to Congressional concern that NIH wasn't doing enough strategic planning and investing in multidisciplinary research, said NIH Deputy Director Raynard Kington at the March 13 joint meeting of NCI's Board of Scientific Advisors and Board of Scientific Counselors.

NIH didn't develop a strategic plan for an obesity initiative until 2004, more than 10 years after public health warnings indicating obesity as an increasing health problem in the U.S., Kington said. While institutes had done some research, "what was missing was a comprehensive integration across NIH to make sure we were making the right investments in this critical area," he said.

"We see OPASI as a novel approach to functionally address a problem that some in Congress and others have suggested should be dealt with by structurally changing NIH," Kington said.

Kington serves as acting director of OPASI, which will report to the NIH director. OPASI will "institutionalize the NIH Roadmap process" to select areas of research, he said.

The common fund that OPASI will allocate to trans-NIH initiatives will be set at 1.6 percent of the appropriations of the institutes and centers for FY 2007. NIH will not increase the percentage until the annual NIH budget increase exceeds the Biomedical Research and Development Price Index. The rate of growth will be determined annually by the NIH director and the IC directors, up to a maximum of 5 percent.

"The goal is not to disrupt funding streams at ICs, but to enhance" support for important research areas, he said.

Selection of research for OPASI funding will begin with proposals by scientists or ICs and advocates. The OPASI staff will review the proposals, and the IC directors and NIH director will further review the list. The list will go to a new "Council of Councils," consisting of about 30 members drawn from nominations from the ICs and the NIH director.

Initiatives would be funded for up to five years, with option for five-year renewal or transfer to an IC.

ICs would still be able to jointly fund initiatives on their own, Kington said.

NCI Programs:

Advisors Approve Renewal Of Cancer Research Network

NCI advisors approved the institute's plan to renew funding for the Cancer Research Network, a $30-million, five-year program that supports research in health maintenance organizations that cover 10 million U.S. residents.

The NCI Board of Scientific Advisors earlier this month unanimously approved the reissuance of a Request for Applications for the program, which supports one grant for an administrative core that

connects established academic research groups with 12 healthcare delivery organizations.

The CRN was funded in 1999 and renewed in 2003. The current funding expires next year. Martin Brown in the NCI Division of Cancer Control and Population Sciences is the program director for the grant.

* * *

Margaret Tucker, chief of the Genetic Epidemiology Branch, was appointed director of the Human Genetics Program in the Division of Cancer Epidemiology and Genetics. She will continue to serve as chief of GEB.

Since joining NCI in 1978, her work has focused on population-based studies of melanoma and other cancers to identify susceptibility genes and gene-environment interactions. She was named chief of the Family Studies Section in 1987 and became chief of GEB in 1992.

* * *

NCI has established the John P. Hartinger Executive Leadership Development Award, a scholarship that will be competitively awarded to an NCI employee who demonstrates leadership potential, a commitment to public service, and a desire to further his or her executive development.

The award honors NCI's associate director for Budget and Financial Management, John Hartinger, a 38-year employee of the institute. NCI Director Andrew von Eschenbach announced the award at the institute's "all-hands meeting" March 7.

At the meeting, six institute employees received NCI Director Gold Star Awards in recognition of special accomplishments: Christine Berg, Division of Cancer Prevention; Donna Bonner, Publications Support Branch; Christina Bruce, Office of Workforce Development; Steve Libutti, Center for Cancer Research; Linda Weiss, Cancer Centers Branch; and Jonathan Wiest, Center for Cancer Research.

* * *

The National Cancer Advisory Board approved new application receipt and review schedules for the Specialized Programs of Research Excellence.

NCI will open all future SPORE receipt dates for the submission and receipt of new, competing continuations, and amended/revised applications for all 14 organ sites and disease groups starting Sept. 20, 2006 (formerly Oct. 1).

On that date, the program will welcome applications from the following organ sites/disease groups: brain, breast, head & neck, gastrointestinal, genitourinary (excluding prostate), gynecological (excluding ovarian), leukemia, lung, lymphoma, myeloma, ovarian, pancreatic, prostate, and skin. Applications will still be received three times yearly, and NCI anticipates that all future receipt dates will be open to all 14 organ sites and disease groups.

Investigators with unfunded applications following peer review will be allowed to revise and resubmit their applications at the next available opportunity and will no longer have to wait for a specific receipt date for each of the organ sites. Further information is available at http://grants.nih.gov/grants/guide/notice-files/NOT-CA-06-021.html.

Funding Opportunities:
Program Announcements

PAS-06-205: Understanding and Treating Tuberous Sclerosis Complex. NCI and other institutes invite R03 grant applications on molecular genetic, developmental, and pathophysiological studies, preclinical therapy development and clinical research in TSC. The PAS is available at http://grants.nih.gov/grants/guide/pa-files/PAS-06-205.html. Inquiries: For NCI--Mary Ellen Perry, 301-496-7028; mp372j@nih.gov.

PAS-06-206: Understanding and Treating Tuberous Sclerosis Complex. Same as above for R21 applications. Text available at http://grants.nih.gov/grants/guide/pa-files/PAS-06-206.html.

PAS-06-207 Interactions Between Stem and Progenitor Cells and the Microenvironment. NIH invites R03 applications for studies on cellular and molecular signaling between the local environment within organisms and stem and progenitor cells introduced as transplants or normally resident within host tissues and organs. NCI is interested in the role of neural tumor stem cells in the progression and development of tumors of the nervous system, with particular emphasis on interaction of the neural tumor microenvironment on the proliferation and differentiation of neural tumor stem cells. Text available at http://grants.nih.gov/grants/guide/pa-files/PAS-06-207.html. Inquiries: For NCI--R. Allan Mufson, 301-496-7815; am214t@nih.gov.

PAS-06-208: **Interactions Between Stem and Progenitor Cells and the Microenvironment.** Same as above for R21 applications. Text available at http://grants.nih.gov/grants/guide/pa-files/PAS-06-208.html.

PAS-06-201: Understanding and Preventing Brain Tumor Dispersal. NIH seeks R21 applications for studies that identify the properties of brain tumor cells that cause them to migrate; determine how interaction of tumor cells with normal brain elements affects migration; and translate understanding of the parameters into interventions that target invading tumor cells. Text available at http://grants.nih.gov/grants/guide/pa-files/PAS-06-201.html. Inquiries: For NCI--Claudio Dansky Ullmann, 301-435-9065; danskyullc@mail.nih.gov.

In Brief:

ASCO Foundation To Fund Geriatric Oncology Awards

(Continued from page 1)

training programs for physicians. To date, 12 fellows have completed the training programs and are eligible for board certification in oncology and geriatrics, and another 18 trainees will be eligible upon completion of the program. The new grant will build on the momentum of the initial program by providing this first generation of geriatric oncology specialists with resources to begin independent research careers, said **Hyman Muss**, principal investigator on the grant and ASCO board member. The grants will fund three types of awards: the Annual Young Investigator Awards; Annual Award and Lecture in Geriatric Oncology; and the B.J. Kennedy Annual Award and Lecture for Scientific Excellence in Geriatric Oncology, a new award and lecture to be presented at the 2007-2009 ASCO Annual Meetings. . . . **PATRICIA WEEKS**, vice president of planning and business development at Fox Chase Cancer Center, received the Bayh-Dole award from the Association of University Technology Managers for her leadership, vision, mentoring, service and dedication to AUTM and to the practice of academic technology transfer. She is a past president of AUTM. . . . **ALBERT DE LA CHAPELLE**, co-director of the molecular biology and cancer genetics program at The Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, won the 2006 German Society of Human Genetics Medal of Honor for his work in human genetics. De la Chapelle discovered genetic mutations in acute myeloid leukemia that signal poorer prognosis. . . . **CITY OF HOPE Cancer Center** received a $20 million grant from the Arnold and Mabel Beckman Foundation to establish the Arnold and Mabel Beckman Center for Cancer Immunotherapeutics and Tumor Immunology. The center will provide space and resources for researchers in the Division of Cancer Immunotherapeutics and Tumor Immunology, said **Michael Friedman**, president and chief executive officer, City of Hope. . . . **UNIVERSITY OF CALIFORNIA, Irvine**, will receive $24 million over five years from the National Center for Research Resources for Function BIRN, a collaboration with 14 institutions to develop and test interdisciplinary techniques for functional magnetic resonance imaging across multiple sites. **Steven Potkin**, professor of psychiatry and the Robert R. Sprague Director of Brain Imaging at UCI, directs Function BIRN.

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THE CANCER LETTER

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Business & Regulatory Report

Product Approvals & Applications:

FDA Approves Taxotere In Combination With Cisplatin, 5-FU, For Gastric Cancer

Sanofi-aventis of Bridgewater, NJ, said FDA has approved Taxotere (docetaxel) in combination with cisplatin and 5-FU for advanced gastric cancer, including cancer of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease.

The additional new application is also currently under review by the Committee for Medicinal products for Human Use of the European Agency for the Evaluation of Medicinal Products.

FDA based its decision on results from the TAX 325 study, an

(Continued to page 2)

Oncology Management:

US Oncology Holdings Reports $19 Mill. Net Income On $2.5B Revenue For 2005

US Oncology Holdings Inc. of Houston, the parent company of US Oncology Inc. reported revenue of $2,518.6 million and net income of $19.1 million for the year ended Dec. 31, 2005.

Last year, revenues were $2,259.8 million and revenues 48.1 million.

Adjusted EBITDA for 2005 was $238.8 million, compared to $259.7 million in 2004. These decreases are primarily due to reductions in Medicare reimbursement relating to the company's medical oncology services segment, the company said.

The decrease in net income is a result of increased interest expense and a reduction in EBITDA, the company said. In 2004, the company incurred merger-related charges and debt extinguishment losses aggregating $56.2 million that did not recur in 2005.

In 2005, medical oncology service revenue increased 11.6 percent, while medical oncology services EBITDA decreased 12.6 percent. Similar to the 2005 quarterly trends, performance was impacted by implementation of ASP reimbursement, partially offset by growth in medical oncology patient visits and pharmaceutical revenue.

"Rapid growth in the cancer patient population and the escalating cost of caring for those patients demand a viable and immediate solution to meet the needs of patients, physicians and payers," said Dale Ross, CEO and chairman of US Oncology. "Our 2006 initiatives demonstrate our continued focus on enabling high quality, cost effective cancer care."

The company said its strategic initiatives are:

(Continued to page 3)

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Sanofi's Taxotere Approved By FDA For Gastric Cancer

(Continued from page 1)

international phase III trial in previously untreated advanced stomach cancer, involving 445 patients.

Patients treated with the Taxotere-based chemotherapy regimen (Taxotere plus cisplatin and 5-FU, or TCF) experienced a significant 23 percent reduction in the risk of death compared to patients who received a current standard treatment of cisplatin and 5-FU (CF). The median follow-up was 23 months.

The median overall survival was significantly longer with the Taxotere-containing regimen (9.2 vs 8.6 months, p=<0.02) with a hazard ratio of 1.29 (95% CI: 1.04-1.61). Time to disease progression was nearly two months longer in the Taxotere- containing arm (5.6 vs 3.7 months, p=0.0004), hazard ratio 1.47 (CF/TCF 95% CI/ 1.19 -1.83).

Locally advanced or metastatic stomach cancer has a poor prognosis with the long-term survival of 11.5 percent. The study's primary endpoint was time to tumor progression (TTP), which was significantly improved with Taxotere based therapy (5.6 months) compared to standard treatment (3.7 months) with a 32 percent reduction in the risk of progression (log-rank test p=0.0004).

The main secondary endpoint was overall survival. Other secondary objectives included response rate, time to treatment failure, duration of response, safety profiles, quality of life and disease related symptoms.

In total, 81.4 percent of the patients experienced at least one Grade 3-4 side effect with the Taxotere-based regimen versus 75.4 percent in the control arm, with neutropenia being the most common Grade 3-4 side effect in the Taxotere-based regimen.

The most common side effects associated with the Taxotere-based regimen were anemia, neutropenia, diarrhea, and nausea. The most common side effects associated with the cisplatin and 5-FU arm were anemia, neutropenia, nausea and vomiting. Primary prophylactic use of growth factor support (G-CSF) was not allowed per protocol.

In the Taxotere arm, febrile neutropenia and neutropenic infection occurred in 12 percent of patients receiving secondary prophylactic G-CSF compared to 28 percent who did not, which represents a 57 percent reduction.

With this indication, Taxotere is approved for six indications in the U.S. in four different tumor types. These include locally advanced or metastatic breast cancer after failure of prior chemotherapy, in combination with doxorubicin and cyclophosphamide (TAC regimen) for the adjuvant treatment of operable, node-positive breast cancer.

In non-small cell lung cancer, Taxotere is approved in combination with cisplatin for unresectable, locally advanced or metastatic non-small cell lung cancer in patients who have not received prior chemotherapy and as a single agent for the treatment of locally advanced or metastatic NSCLC after failure of prior platinum-based chemotherapy.

Also, Taxotere is approved for use in combination with prednisone for androgen-independent metastatic prostate cancer.

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American Pharmaceutical Partners Inc. (Nasdaq: APPX) of Schaumburg, Ill., said it has received two tentative approvals from FDA for its aNDAs for Ondansetron Injection, USP, single-dose and multiple-dose vials, the generic equivalent of the GlaxoSmithKline Zofran Injection.

Ondansetron Injection is indicated for the prevention of nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including high-dose cisplatin, and prevention of postoperative nausea and/or vomiting, the company said.

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Bioenvision (Nasdaq: BIVN) of London said the European Medicines Agency Committee for Medicinal

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Products for Human Use has adopted a positive opinion on the Marketing Authorization Application for Evoltra (clofarabine).

The drug is indicated for acute lymphoblastic leukemia in pediatric patients who have relapsed or are refractory to at least two prior regimens.

The CHMP opinion would now be converted into a marketing authorization by the European Commission, a process that is expected to take up to 3 months, at which time Bioenvision said it would launch Evoltra throughout Europe.

"Pediatric hematologists would be very interested by the CHMP positive opinion," said André Baruchel, head of the Department of Pediatric Haematology, Hôpital Saint-Louis, Paris. "Achieving a 20 percent to 30 percent overall response rate, which can be durable, in children and adolescents with ALL who have relapsed or are refractory, is very promising."

Evoltra (clofarabine) is a next generation purine nucleoside analogue, the company said. Clofarabine has been granted orphan drug designation for both ALL and AML in the U.S. and Europe. In Europe, the designation provides marketing exclusivity for 10 years following marketing authorization.

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Celgene Corp. (Nasdaq: CELG) of Summit, N.J., said FDA has granted a Priority Review designation to its sNDA for Revlimid (lenalidomide) for relapsed or refractory multiple myeloma.

The company said it is seeking approval to market the drug in combination with dexamethasone for multiple myeloma where at least one prior therapy, subject to FDA review and approval, was given, the company said.

The sNDA submission is based on two randomized phase III special protocol assessment trials, North American Trial MM-009 and International Trial MM-010, evaluating Revlimid plus dexamethasone, the company said. Both studies achieved the primary endpoint of time to disease progression with combination therapy of lenalidomide and dexamethasone over that of placebo and dexamethasone.

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ChemGenex Pharmaceuticals Ltd. (Nasdaq: CXSP) of Melbourne, Australia, said FDA has granted Orphan Drug status to Ceflatonin for chronic myeloid leukemia.

Ceflatonin induces apoptosis in myeloid cells and inhibits angiogenesis, the company said. Ongoing or soon to be initiated studies would evaluate the drug for conditions including chronic myeloid leukemia, myelodysplastic syndromes and acute myeloid leukemia, the company said.

The agent was given a similar designation by the European Union in 2004, based on a positive recommendation by the Committee for Orphan Medicinal Products of the European Medicines Agency, the company said..

Ceflatonin has confirmed phase II activity in resistant CML, both as a single agent and in combination with other approved drugs, the company said.

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Viragen Inc. (AMEX: VRA) of Plantation, Fla., said the Swedish Medical Products Agency approved Multiferon (multi-subtype, natural human alpha interferon) for first-line adjuvant treatment of stages IIb- III malignant melanoma following dacarbazine after surgical removal of tumors.

Approval for Multiferon in sequential combination with DTIC was granted based on clinical trial data that demonstrated a statistically significant advantage over untreated controls in terms of survival-without-distant-metastasis and overall survival, the company said.

"In coordination with our expert Melanoma Advisory Board, we have initiated the process to conduct a post-marketing supporting clinical trial with Multiferon on a pan-European basis," said Charles Rice, president of Viragen. "The trial is scheduled to include up to 1,000 patients in multiple centers across Europe and is expected to build additional clinical evidence of the value of Multiferon in cancer therapy."

Multiferon is a highly purified, multi-subtype, natural human alpha interferon, the company said.

Oncology Management:

US Oncology Outlines "Strategic Initiatives"

(Continued from page 1)

—"Increase the financial strength of network practices by expanding their service offerings, consolidating their market position in their geographic markets and supporting clinical initiatives that help ensure the continued delivery of high quality and effective cancer care to their patients.

—"Enhance the network's ability to deliver high quality cancer care and to lower the overall operating costs through the company's ongoing quality improvement program, which includes: accelerating the installation of iKnowMed, the company's oncology-specific electronic medical records system into network practices; supporting the implementation of an evidence-

based approach to treatment decisions; and creating Centers of Excellence that bring increased focus and attention to specific areas of cancer care.

—"Provide the payer community with a cost-effective, high quality cancer care model based upon exceptional clinical insight, cost benchmarking, and demonstrated, measurable clinical outcomes for patients. In 2005, the company established a clinical outcomes group and would continue to build upon those capabilities in 2006.

—"Expand the company's relationships with the manufacturers of oncology pharmaceuticals and equipment to increase the convenience, safety and clinical effectiveness of their products through the continued expansion of the company's manufacturing and distribution services, including the 2006 launch of the OncologyRx Care Advantage specialty pharmacy distribution business."

In August 2004, US Oncology became a wholly owned subsidiary of holdings in a merger transaction valued at approximately $1.6 billion. The holding company is owned by Welsh, Carson, Anderson & Stowe IX, L.P.

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Coalition of Cancer Cooperative Groups of Philadelphia said it has launched QuickLink, a colorectal cancer clinical trial resource for patients, caregivers and people at risk.

QuickLink provides information on ten of the largest colorectal trials available, along with links to patient support services and access to the screening capabilities of TrialCheck, the Coalition database and navigator of thousands of cancer clinical trials, the group said. TrialCheck offers a way to locate trials, with results displayed by proximity to the user's Zip Code.

"As a direct outcome from clinical trials, five new drugs have received FDA approval over the last five years making new and better treatments more available to patients with colorectal cancer today than ever before," said Robert Comis, president of the coalition. "There are many trials available for prevention, screening and early detection of colorectal cancer or pre-cancerous polyps."

QuickLink can be found at http://www.cancertrialshelp.org/.

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Emageon Inc. (Nasdaq: EMAG) of Birmingham, Ala., said it has entered into a digital healthcare information management agreement with **H. Lee Moffitt Cancer Center**.

"The Emageon EVMS system would consolidate DIC images and deliver advanced visualization toolsets to our clinicians," Edward Martinez, vice president and chief information officer of Moffitt Cancer Center, said in a statement. "This parallels our vision to have a seamless relationship among clinical results, genomic and scientific data, and images (2D, 3D, and 4D), allowing clinicians and researchers to properly review all the data associated with the case at hand."

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OTN of South San Francisco and **Onmark,** an OTN company, said the Midwest Oncology Practice Society has selected them to provide oncology services to its members.

MOPS represents 21 private oncology practices at 38 sites in Nebraska and Iowa, the companies said. The two-year agreement, worth $120 million, covers drug distribution, technology and GPO services, the company said.

Under the agreement, the MOPS members will have access to OTN distribution and specialty pharmacy services; pricing; technology, including Lynx Station, Lynx Practice Manager and the Lynx Mobile inventory management system; comprehensive medical/surgical supplies; and practice management tools, the companies said.

With the addition of MOPS, Onmark said it has enrolled more than 1,500 medical practices since launching 15 months ago, the company said.

Clinical Trials:

Novartis Begins Adjuvant Femara Vs. Arimidex Trial

Novartis of East Hanover, N.J., said it has begun a trial of its aromatase inhibitor, Femara (letrozole tablets) vs. Arimidex (anastrozole) as adjuvant therapy for breast cancer.

The Femara vs. Anastrozole Clinical Evaluation, or FACE, trial would define the optimal adjuvant treatment in postmenopausal women with node-positive early breast cancer, the company said.

FDA approved Femara as initial adjuvant treatment for postmenopausal women with hormone-sensitive early breast cancer, the company said.

Femara has demonstrated greater benefit than tamoxifen in reducing the risk of breast cancer recurrence, the company said. The benefit was particularly strong in women with a higher risk of their cancer coming back.

"The FACE trial is an important tool to evaluate the benefit of Femara in women at increased risk for

recurrence in a randomized comparison to anastrozole," said Diane Young, vice president and global head of clinical development at Novartis Oncology.

"For many years, practicing oncologists have asked for comparative data on the two leading aromatase inhibitors to help guide treatment choice, especially for patients who are more likely to experience a recurrence," said Kathleen Pritchard, professor of medicine at the University of Toronto and lead investigator.

FACE is a global phase III randomized multi-center study involving more than 250 trial sites comparing the efficacy and safety of Femara to anastrozole, with an expected enrollment of 4,000 node-positive postmenopausal women with hormone-sensitive early breast cancer, one quarter will be enrolled in the U.S., the company said.

The primary endpoint is disease-free survival, the company said. Participants also may have received adjuvant chemotherapy post-surgery. Other outcomes to be evaluated include overall survival, distant metastases and contralateral breast cancer. Efficacy results are expected in approximately four to five years, while safety data may be available in 2009.

Arimidex is sponsored by AstraZeneca.

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BiPar Sciences Inc. of Brisbane, Calif., said it has begun enrollment in a phase I trial of BSI-201, for advanced malignancies.

The drug, an inhibitor of PARP (poly-adenyl-ribose polymerase), a regulator of gene transcription and DNA repair, has been shown to be well tolerated and has exhibited activity against a range of tumor types, including ovarian, prostate, breast, colon, lung, pancreatic, cervical and bladder, the company said.

The open-label, dose-escalation clinical study would be conducted at M.D. Anderson Cancer Center, and the Institute for Drug Development in San Antonio, the company said.

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CuraGen Corp. (Nasdaq: CRGN) of Branford, Conn., and **TopoTarget A/S** (Copenhagen Stock Exchange: TOPO) announced the initiation of patient dosing in a phase I trial of PXD101, a small molecule histone deacetylase (HDAC) inhibitor, in combination with Velcade (bortezomib) for advanced malignancies, including solid tumors and lymphomas.

The trial is being sponsored by NCI under a Clinical Trials Agreement with CuraGen for PXD101 and under a Cooperative Research and Development Agreement with Millennium Pharmaceuticals Inc. for bortezomib.

NCI-sponsored clinical trials with PXD101 are conducted in parallel to those clinical trials sponsored by CuraGen, including the phase Ib/II study of PXD101 plus Velcade (bortezomib) for the treatment of multiple myeloma initiated last week by CuraGen and TopoTarget.

The phase I trial is an open-label, dose-escalation study being led by S. Gail Eckhardt, director of the developmental therapeutics and GI malignancies programs and professor of medicine at the University of Colorado Health Sciences Center.

Up to 36 patients will be enrolled in the dose escalation portion of the study and receive PXD101 and bortezomib in a three week cycle. Following determination of the MTD, the study will enroll 10 additional patients to further assess the biologic activity of PXD101 and bortezomib against tumor cells, including inhibition of HDAC and the proteasome.

PXD101 is a small molecule HDAC inhibitor being investigated for its role in the treatment of a wide range of solid and hematologic malignancies either as a single-agent, or in combination with other active anti-cancer agents.

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Delcath Systems Inc. (Nasdaq: DH) of Stamford, Conn., said it has completed a Special Protocol Assessment and Agreement with FDA for metastatic melanoma in the liver using the Delcath system with melphalan, an approved anticancer agent.

The company said it would begin a phase III trial at NCI.

Under the SPA, the company said it is required to complete one phase III trial in order to file a Premarket Approval application. The randomized, multi-center trial would enroll 92 patients diagnosed with ocular and cutaneous melanoma metastatic to the liver. Randomization would be either to the Delcath system using melphalan or a control group receiving best alternative care.

The control group would be reviewed on a case-by-case basis and receive an existing treatment option deemed most appropriate by the principal investigator, the company said.

The primary endpoint is whether using the Delcath system would result in a reduction in tumor burden or zero progression of the metastatic melanoma in the liver for a longer period versus receiving best alternative care, the company said.

Participants randomized to the control group whose tumors are found to progress would be allowed to cross over and receive treatment using the Delcath

system. Results from the point of crossover would not impact the study.

"Due to the positive results from the phase I study conducted at NCI, and building on results achieved with melphalan via a surgical approach, we have received a number of referrals of qualified patients nationwide to participate in the upcoming phase III trial," James Pingpank Jr., principal investigator for the NCI trial. "Our plan is to begin the active enrollment of patients into this study effective immediately.

The Delcath system delivers high-dose chemotherapy directly to the liver via the hepatic artery, the company said. As blood exits the liver, special Delcath filters trap the chemotherapy, protecting the rest of the body from excessive toxicity.

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Eli Lilly and Co. of Indianapolis said it has begun a phase III study of Enzastaurin, an investigational, targeted, oral agent for relapsed glioblastoma multiforme at more than 100 sites worldwide.

The enzastaurin glioblastoma phase III trial, known as the STEERING Study, is a randomized, open label registration study in recurrent GBM, which would compare the efficacy, safety and tolerability of enzastaurin, taken orally, versus CeeNU (lomustine), the company said

Howard Fine, chief of neuro-oncology at NCI, is the principal investigator for the study that would enroll 397 patients, the company said. The primary endpoints would be progression-free survival and overall survival. Lilly said it would analyze tissue samples for biomarkers as a basis for correlating response to clinical trial outcomes.

Enzastaurin is an oral serine-threonine kinase inhibitor that suppresses tumor growth through multiple mechanisms, the company said. The agent has been granted orphan drug designation for glioblastoma by the European Agency for the Evaluation of Medicinal Products and by th"e FDA, the company said.

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Halozyme Therapeutics Inc. (AMEX: HTI) of San Diego said it has completed enrollment in a phase I trail for its investigational recombinant therapeutic Chemophase for superficial bladder cancer.

The clinical protocol evaluated a single intravesical administration of the treatment along with mitomycin, the company said. The study was conducted at BCG Oncology in Phoenix under the supervision of Donald Lamm, principal investigator.

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Keryx Biopharmaceuticals Inc. (Nasdaq: KERX) of New York said it has begun a corporate-sponsored phase II, multi-center program to evaluate KRX-0401 (perifosine) for leukemia.

The principal investigator is Frank Giles, chief of developmental therapeutics, Department of Leukemia at M.D. Anderson Cancer Center, the company said.

The trial would assess the objective response rate and evaluate the pharmacokinetics and safety and tolerability of the product as a single agent in relapsed or refractory acute myeloid leukemia, acute lymphocytic leukemia, chronic lymphocytic leukemia, high-risk myelodysplastic syndrome and chronic myeloid leukemia in the blastic phase, the company said.

The company said it would begin additional hematological studies, including another corporate-sponsored DFCI-led phase I/II study evaluating the safety and efficacy of KRX-0401 and Velcade (bortezomib) therapy with or without dexamethasone for relapsed or refractory multiple myeloma previously treated with bortezomib.

KRX-0401is in-licensed by Keryx from AEterna Zentaris Inc. (TSX: AEZ; Nasdaq: AEZS), in the U.S., Canada and Mexico, the company said.

KRX-0401 modulates AKT and other signal transduction pathways, including the MAPK and JNK pathways, the company said. Perifosine has shown single agent partial responses or long term disease stabilizations in solid tumors including sarcoma and prostate cancer.

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RxKinetix Inc. of Boulder, Colo., said it had concluded the "end of a phase II meeting" with FDA for RK-0202 in oral mucositis and is proceeding with phase III development of the agent.

The company's phase II double-blind, randomized and placebo controlled trial demonstrated efficacy with patients receiving RK-0202 having a 29 percent lower incidence of WHO Grade 3 or greater oral mucositis versus placebo at 50 Gy ($p = 0.041$) and a 46 percent lower incidence of NCI Grade 3 or greater oral mucositis versus placebo at 50 Gy ($p = 0.0052$).

Fewer patients on RK-0202 required an external feeding tube compared with placebo ($p = 0.037$). Those receiving RK-0202 also had lower incidence of adverse events such as weight loss, anorexia, dry mouth, nausea and dehydration, the company said.

RK-0202 is comprised of the antioxidant N-acetylcysteine in a polymer matrix based on the RxKinetix ProGelz technology, the company said.

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Sunesis Pharmaceuticals Inc. (Nasdaq: SNSS) of

South San Francisco said treatment has begun in a phase II trial of its agent SNS-595 for small cell lung cancer.

The trial is an open-label, multi-center study examining the safety and efficacy of SNS-595 as a second-line agent in small cell lung cancer where first-line therapy has failed, the company said.

SNS-595 is a first-in-class cell-cycle modulator that induces apoptosis, as cells progress through the S phase of the cell cycle, the company said.

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Telik Inc. (Nasdaq: TELK) of Palo Alto said it has begun a multicenter phase I/IIa study to evaluate the tolerability and pharmcokinetics of Telintra Tablets for myelodysplastic syndrome.

In a completed phase II trial of the parenteral formulation of Telintra in MDS, data demonstrated high levels of Hematologic Improvement assessed by the standard International Working Group MDS response criteria, including bilineage and trilineage HI, the company said. Responses were observed across all MDS FAB types and in low, intermediate and high risk MDS.

Telintra is a small molecule product candidate that has demonstrated myelorestorative activity when administered orally or by infusion in preclinical testing, the company said.

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Wyeth Pharmaceuticals Madison, N.J., said it would discontinue the Horizon phase III trial program of Temsirolimus oral tablets, its investigational drug, in combination with Femara (letrozole) for first-line use in postmenopausal women with hormone-receptor positive metastatic breast cancer.

The decision was based upon the recommendation of an Independent Data Monitoring Committee after review of data from a planned interim analysis, the company said.

The study compared the combination of Temsirolimus oral tablets and letrozole versus letrozole alone, the company said. The IDMC advised that continuation of the trial was unlikely to achieve the targeted level of efficacy for the combination therapy compared to letrozole alone.

While the phase III trial for women with hormone-receptor positive metastatic breast cancer involved an oral formulation of Temsirolimus, two other phase III trials studying Temsirolimus in renal cell carcinoma and mantle cell lymphoma using an intravenous formulation are continuing, the company said. About the IDMC and the Interim Analysis.

Temsirolimus inhibits mTOR, mammalian target of rapamyci, kinase, a protein in tumor growth and cell survival, the company said

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YM BioSciences Inc. (AMEX: YMI)(AMEX: TSX: YM)(AMEX: AIM: YMBA), of Mississauga, Ontario, said its partner, **Oncoscience AG**, has been cleared by the German regulatory authority for biological products, the Paul Ehrlich Institute, to initiate a phase III trial of nimotuzumab in combination with radiation in children with inoperable pontine glioma.

The trial was also reviewed with the EMEA and is designed as a prospectively registrable study on the basis of a single arm trial because of the absence of treatment options for children suffering from pontine glioma.

The trial is a single arm study in which 40 children with inoperable pontine glioma will be treated with radiation concomitant with nimotuzumab. The primary clinical endpoints in the trial will be progression-free survival at 3, 6, 12 and 24 months with median survival as secondary endpoint.

Clinical sites will be located in Germany, Italy, Belarus and Russia and it is anticipated that recruitment could be completed within approximately 12 months after the start of patient enrolment. Based on a historical median survival for this form of cancer of approximately 8.5 months, the trial could be completed in the second quarter of 2007.

YM BioSciences said it plans to file for authorization to conduct a phase III trial in North America following a clearance for such a trial in Germany.

In addition, YM said it would pursue the clinical development of nimotuzumab in adult glioma as well as the current target of non-small cell lung cancer. YM's licensor, CIMAB SA and its parent, the Center for Molecular Immunology, are conducting trials with nimotuzumab in glioma, breast, esophageal, cervical, prostate and head and neck cancer.

Deals & Collaborations:

Infinity, Novartis In Alliance On Developing Bcl-2 Drugs

Infinity Pharmaceuticals Inc. of Cambridge, Mass., said it has entered into a global strategic alliance with **Novartis** for drugs targeting Bcl-2 protein family members for cancer indications.

Under the agreement, Infinity said it would receive $30 million in upfront license fees, an equity investment and committed research funding over the first two years of the relationship. Along with success-based milestones, total payments to Infinity could exceed

$400 million, the company said. Infinity said it would receive royalties upon successful commercialization of products developed in the alliance. Novartis would invest in an Infinity public offering, should it occur within two years.

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Chemokine Therapeutics Corp. (OTCBB: CHKT; TSX: I) of Vancouver said it has entered into an agreement with **M. D. Anderson Cancer Center** to study the Chemokine compound, CE-9908, a chemokine CXCR4 antagonist.

Researchers would study the ability of the drug to inhibit metastasis in breast cancer in preclinical models, the company said.

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Diosynth Biotechnology of Research Triangle Park, N.C., said it has entered into a long-term commercial supply agreement with **Dendreon Corp**. (Nasdaq: DNDN) for the manufacture of the recombinant antigen component Provenge (sipuleucel-T), the Dendreon investigational active cellular immunotherapy for prostate cancer.

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Isis Pharmaceuticals Inc. (Nasdaq: ISIS) of Carlsbad, Calif., and **Rosetta Genomics Ltd**. of Rehovot, Israel, said they have entered into a joint collaboration for hepatocellular carcinoma research.

The collaboration would bring together the expertise of both companies in miRNA and leverage the Rosetta database of miRNA genes and the Isis expertise in oligonucleotide chemistry and antisense drug discovery and development, the companies said.

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Millennium Pharmaceuticals Inc. (Nasdaq: MLNM) of Cambridge, Mass., said it would receive a $10 million payment from **Johnson & Johnson Pharmaceutical Research & Development**, **L.L.C**. based on sales milestones reached for Velcade (bortezomib) for Injection outside the U.S.

In June 2003, Millennium entered into an agreement with Ortho Biotech Products, L.P. and its research affiliate, J&JPRD, to develop and commercialize the drug, the company said.

Under the agreement, Ortho Biotech and its affiliate, Janssen-Cilag, would commercialize Velcade outside of the U.S. and Millennium would receive royalties on sales outside the U.S. Millennium would receive payments for achieving clinical, development and regulatory approvals and sales milestones outside of the U.S.

Velcade is indicated for multiple myeloma patients who have received at least one prior therapy, the company said.

In a related development, Millennium Pharmaceuticals Inc. and J&JPRD said they have begun a three-arm, randomized, phase II study of Velcade and pemetrexed for locally advanced or metastatic non-small cell lung cancer where prior chemotherapy treatment has failed.

The study would assess the additive benefits of combining the activity of two targeted therapies with different mechanisms of action, the companies said. Also already underway is a two-arm, randomized, phase II study of Velcade in combination with erlotinib for locally advanced or metastatic NSCLC and a study of single-agent Velcade in relapsed bronchioalveolar carcinoma and adenocarcinoma of the lung.

The three-arm phase II randomized, open-label, multi-center study would enroll 135 patients, the companies said. The primary endpoint is objective response rate as assessed by Response Evaluation Criteria in Solid Tumors criteria.

Secondary endpoints include disease control rates, time to progression, progression-free survival and safety. The three treatment groups consist of the following treatments: Velcade in combination with pemetrexed, pemetrexed alone or Velcade alone.

Velcade would be administered on a weekly schedule in both arms. The weekly dose of Velcade in this study is 1.6 mg/m2 and pemetrexed would be administered at the standard registered dose of 500 mg/m2, the companies said.

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Spectrum Pharmaceuticals Inc. (Nasdaq: SPPI) of Irvine, Calif., said it has entered into a definitive agreement to acquire the oncology drug assets of **Targent Inc.**

Spectrum said it would obtain levofolinic acid, the pure active isomer of calcium leucovorin, a component of 5-FU containing regimens for colorectal cancer and other malignancies. Calcium leucovorin is also used after the administration of high-dose methotrexate in treating certain malignancies.

An NDA for the drug has been filed with FDA for the osteosarcoma indication, the company said. LFA has been granted orphan drug status for colorectal cancer in combination with 5-FU and for osteogenic sarcoma in use with metheotrexate rescue.

Wyeth, Sanofi-Aventis and others market LFA, which includes Europe and Japan, while Spectrum said it would obtain the rights in the U.S., Canada and Mexico.