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NCI Begins Cancer Center Grant Rewrite, Will Allow Clinical Investigator Support

NCI is rewriting the guidelines for Cancer Center Support Grants to implement changes recommended by an advisory group last year, Institute officials said earlier this week.

Changes in the works for the $217-million grants program which funds core resources at NCI-designated cancer centers include:

--The addition of salary support for clinical investigators who engage in clinical trials.

--More support for tissue banks, data management, and regulatory compliance.

--Credit for centers that work with other NCI-funded networks,

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In Brief:

John Mendelsohn Selected For BMS Award; M.D. Anderson To Receive $25 Million Gift

JOHN MENDELSOHN will receive the 27th annual Bristol-Myers Squibb Freedom to Discover Award for Distinguished Achievement in Cancer Research. Mendelsohn, president of M. D. Anderson Cancer Center, was recognized for his work in cancer education, research, and treatment, and for his discoveries on inhibiting cancer cell growth. He is known for developing, along with his colleague **Gordon Sato**, a series of monoclonal antibodies, including monoclonal antibody 225, that specifically bind to and inhibit the epidermal growth factor receptor. The research efforts led to the development of therapies including cetuximab, a modified, chimeric human-mouse monoclonal antibody. Cetuximab is now known as Erbitux. The award, a $50,000 cash prize and a silver commemorative medallion, will be presented to Mendelsohn on Oct. 14. . . . **M. D. ANDERSON Cancer Center** has received a $25 million gift from the estate of the late Houston philanthropist and art collector **Caroline Wiess Law**. The funds will support two research initiatives in the Division of Cancer Prevention and Population Sciences. One of the initiatives, led by **Bernard Levin**, vice president of cancer prevention, will explore molecular techniques for the prevention and early detection of colorectal adenomatous polyps and cancer. The gift also will fund a multidisciplinary research program aimed at cancer prevention. The program will integrate emerging approaches such as bio-behavioral science, molecular epidemiology, and the study of health disparities with the research areas of epidemiology, behavioral science, clinical cancer prevention, and basic science. Part of the funds will be used to enhance

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NCI Plans To Rewrite, Simplify Cancer Center Guidelines

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such as cooperative groups and Specialized Programs of Research Excellence.

--Optional site visits for centers in renewal that do not have a new director or seek a greater than 10 percent budget increase.

The rewrite also will simplify the 109-page, single-spaced guidelines document, said Karen Antman, an oncologist on assignment to NCI from Columbia University, who is working with the Cancer Centers Branch to revamp the guidelines.

"Michael Milken at a recent meeting observed that modern trains can travel at speed of 300 miles per hour, but, built for a different era, U.S. rails preclude these speeds," Antman said in a presentation March 15 to the NCI Board of Scientific Advisors. "We would like to build a better infrastructure for cancer centers so that we can go at whatever speed the science requires for progress."

Antman was recruited by NCI Director Andrew von Eschenbach to implement the recommendations of the P30-P50 Working Group, which submitted its review of the Cancer Centers Program (P30 grants) and the SPORE program (P50 grants) to NCI in February 2003 (**The Cancer Letter**, Feb. 28, 2003).

Antman served on the working group and was director of the Herbert Irving Comprehensive Cancer Center. Now she is von Eschenbach's choice for deputy director for translational and clinical sciences, one of four new deputy director positions at NCI (**The Cancer Letter**, Feb. 20, 2004).

A draft of the guidelines document is expected to be presented to the National Cancer Advisory Board at its meeting scheduled for June 1. Revisions to the SPORE grant guidelines will follow the cancer center guidelines by a few months, Antman said.

At the BSA meeting, Antman presented a point-by-point response to the working group's recommendations for the Cancer Centers Program, indicating NCI's plans for guideline revisions.

Following is her summary of the report's recommendations and the NCI response:

1.1 Phase out the P20 planning grant.

NCI: The grant program was immediately suspended.

1.2 Cancer centers budget should grow slightly faster than the R01 budget.

NCI: Underway.

2.1 Include cancer center directors in NCI's strategic planning. Allow them to offer guidance in developing new NCI initiatives and disseminating research findings.

NCI: Cancer center directors retreat was held March 8; this will be an annual event. Other strategic planning meetings are being discussed.

2.2 Look to centers as sites to pilot new research and dissemination programs to assure cost-effective integration with existing resources.

NCI: This is already the strategy for many RFA proposals. In the past year, $29.5 million worth of initiatives and grants supplements have been available for the centers. This will continue or increase.

2.3 Allow salary support for clinical researchers who actively engage in trials in recognition of their essential role in translational research.

NCI: Draft guidelines modified to allow staff salary support for clinical investigators. "We made some fairly extensive changes in both the staff investigator paragraphs and the junior staff investigators," Antman said.

2.4. Revise funding of P30 shared resources to provide more appropriate support for critical under-

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funded activities such as tissue banks, data management, and regulatory compliance.

NCI: All are already allowed in tissue bank and clinical trials cores, protocol review monitoring, data and safety monitoring, and data sharing and protocol-specific research. Better instructions will be provided to applicants and reviewers. "We will make clear that these are to be encouraged," Antman said.

2.5 Encourage geographic distribution. Create a new cancer center category for academic institutions unable to meet all P30 requirements; these institutions would be associated with and funded through an existing P30 center.

NCI: Cancer center consortia and affiliations are described in new draft guidelines.

2.6 Provide support for cancer centers actively seeking links with state health departments, other state agencies, or the Centers for Disease Control and Prevention.

NCI: Here funding would presumably be in the prevention and control programs and cores, Antman said. FTE support for outreach used to be in the guidelines, but was removed. "Another way to do this would be supplements or planning grants; however, under the current budget constraints, that may not happen this or next year," Antman said.

2.7 Encourage and support centers to develop infrastructure and test novel methods for disseminating new knowledge in clinical, cancer control, and early detection research.

NCI: "We have written a suggestion for dissemination cores in the guidelines," Antman said. "The request will also go into prevention and control cores. Many institutions are also asking for recruitment cores. This could also be addressed with supplements or planning grants in the future, pending better budgets."

3.1 Support clinical bioinformatics. Make a national clinical research and informatics system a priority. Appropriately integrate with centers, the Association of American Cancer Institutes, industry, and other interested parties.

NCI: "caBIG is a major initiative; it's probably the No. 1 initiative within the NCI currently," Antman said. "That would mean that we probably need to bring more IT people active in review." James Doroshow, of City of Hope, and soon to be director of the NCI Division of Cancer Treatment and Diagnosis, is chairman of an NCI clinical trials committee reviewing the integration of centers, industry, and clinical trials, she said.

3.2 Limit additional review of clinical trials that are supported by previously peer-reviewed funding mechanisms to safety and regulatory issues. Eliminate NCI Cancer Therapy Evaluation Program review of grants or phase I and II studies unless CTEP holds the IND. Impose a 30-day turnaround on those studies requiring review.

NCI: CTEP review applies only to CTEP and Division of Cancer Prevention sponsored agents and cooperative group studies. Review turnaround time is now close to 30 days.

3.3 Work with the federal Office for Human Research Protections to engage cancer center institutional review boards in developing a strategy for centralized review of multi-center trials.

NCI: The NCI Central IRB is in place for phase III trials. Phase II trials are being added. Other consortia are developing central review, such as the University of Pittsburgh single IRB for multiple institutions.

3.4 Streamline review of P30s by eliminating the need for some site visits.

A poll of center directors found that 30 percent don't want site visits, while 70 percent "were adamant about wanting site visits," Antman said. "I think we will put both options into the guidelines so that centers who are eligible, who have done very well in the past and don't have a new center director, could conceivably ask for administrative review going to the parent committee, with a small review committee coming out to do regulatory review of the protocol monitoring system. To decrease the burden for 30 percent of our centers would be a substantial step forward."

The proposed review process would begin with the parent committee conducting initial review of competitive renewals. NCI staff would review administrative and procedural aspects for fiscal accountability. Administrative site visit review would be restricted to issues uncovered by parent committee review or NCI staff. Site visit review would be required for new applicants and centers seeking a greater than 10 percent grant increase.

"In the recent past, virtually every center came in with greater than 10 percent increase, so that wouldn't eliminate anyone; however, in the current fiscal constraints, many would be happy to have that as their request," Antman said.

Antman said it remains unclear how the streamlined review would deal with issues such as proposed new non-research areas, assuring budget accountability, and optimal review of comprehensive status. Also, under the proposed streamlined review, applications must be complete and there is no opportunity to make corrections. In addition, she noted that site visits often improve priority scores.

The new review system would result in increased burden on the parent committee, but decreased time devoted to site visits. Also, administrative and fiscal review by NCI staff departs from NIH peer review procedures, so would probably have to be done by the parent committee.

3.5 Adjust the review process to consider collaborations with P50s, cooperative groups, and participation in networks, community service, outreach, and dissemination.

NCI: Credit in clinical research is given for cooperative group and SPORE participation, but centers would like more credit for taking leadership roles in cooperative groups. Comprehensive status rewards networks, service, outreach, and dissemination.

3.6 Develop quantifiable metrics for determining the size of the P30 award to reflect the broad spectrum of involvement of individual cancer centers in discovery, dissemination, and delivery of care.

NCI: Currently, awards are set at about 15 percent of a center's NCI grant funding, because the 20 percent level is not feasible under the Institute's budget. Possible alternative models include a sliding scale based on NCI funding, a fraction of NCI, NIH, or total peer reviewed funding, a cap set at a specific dollar amount, or allow site visitors to determine the funding level.

"We currently have a system that is site-visitor determined, and based on about 20 percent of NCI funding, just kind of a baseline," Antman said.

A cap in overall funding at $10 million would penalize a few large centers. A 50 percent (or some other level) growth rate cap on current award would penalize small centers. A sliding scale of NCI funding to CCSG such that smaller centers receive a higher ratio is rather complex.

"These are still under discussion, since we haven't really resolved this issue," Antman said.

3.8 Develop a process to describe and quantitate on an annual basis the overall contributions of the P30/P50 program.

NCI: The Institute will ask centers to provide an annual list of accomplishments. This would be used for appropriations.

Renewal schedule: NCI is developing a plan to reschedule the renewal dates of some centers to more evenly distribute the number of centers that compete each fiscal year, Antman said. The goal is to schedule about 12 competitive renewals per year. CCSG receipt dates are Feb. 1, June 1, and Oct. 1.

As currently scheduled, 10 centers will compete in fiscal 2004. Next year, 17 centers are scheduled to go through renewal, and in 2006, 15 centers will compete. However, in 2007, only six centers are scheduled to compete. "It's clear that we have problems," Antman said.

To solve the problem, some of the centers that are scheduled for FY 2005 and 2006 spring renewals will be moved by a few months to up to a year so that they compete in the following fiscal year, she said.

The P30-P50 Working Group report is available at http://deainfo.nci.nih.gov/ADVISORY/ncab/p30-p50/index.htm.

Board Discussion: Problems in Review?

Rewriting the guidelines still may not solve the problem of implementing NCI's vision for the centers program through the review process, said BSA member Robert Young, president of Fox Chase Cancer Center.

"Sixteen years ago, when I ran this program, the central problem was the integration and communication between the program staff and review," Young said at the board meeting.

"Sixteen years later, it's the same central issue. You can define all of the guidelines that you want, but if the review process sets it own set of guidelines, and the site visitors are given that set of guidelines to work with, that's the set of guidelines that will prevail. We really desperately need to try to harmonize the goals of program and review, and I think that still seems to be a challenge."

ANTMAN: "There are the guidelines for review and there's the culture. We can easily change the words in the guidelines for review. The real question is, can we change the culture?"

YOUNG: "Let's be clear about where the culture lies. The culture doesn't lie with the reviewers. Many of the reviewers live in cancer centers. I think they are quite familiar with the guidelines and what the program is trying to accomplish with this tool. That view is not widely held, at least in my view, on the culture of the

review side, from the point of view of the NIH staff."

PAULETTE GRAY, director, NCI Division of Extramural Activities: "During the review process, we actually use the review criteria that are developed by program staff. So, I'm somewhat befuddled as to how in review we have somehow tarnished the overall process. In this new scenario, with Karen here, program and review are working very closely to ensure that the criteria that are now put on paper will be adhered to. So, we will try to make this a team effort, because we are all trying to reach the same goal."

YOUNG: "Let me just say in response that sometimes the cancer centers are befuddled by the apparent inconsistency between what we perceive as the guidelines as generated by program, and the criteria that are used at the time of site visit reviews."

GRAY: "I hear what you are saying, and we will ensure that whatever review criteria are developed by staff, we within the review organization will adhere and implement those specific criteria."

DAVID MASLOW, chief, NCI Resources and Training Review Branch: "I did some analysis of data that indicated that approximately 70 percent of the people on site visits had positions of leadership in cancer centers, not just members. The parent committee always has center directors on it.

"The culture is the cancer center community. I don't understand why people wear a different hat when they are applying than when they are reviewing. Perhaps that's true. At every review, there are program [staff] present who provide guidance if the reviewers stray from the interpretation of the guidelines. I won't argue that the review process is absolutely perfect. It's people, and people may not be perfect, but we do stay very close to the guidelines."

VON ESCHENBACH: "I want to really reinforce the fact that we are taking a very systematic and systems approach to this process. It is important that the tail not be wagging the dog, in the sense that the review process should be reflecting all of the criteria that have been put into what we want to define and shape the cancer program. So first step in this is to get very crisp clarity around that, and embedding that into the review process, mechanism, and instruction to people accordingly. We are not ignoring that, but are beginning this in a systematic way.

"One of the places where the committee is going to be very helpful, is helping to shape the budget and funding mechanisms around these processes in terms of how we grow and define the program, what it is that we are compensating and rewarding, and what pieces of infrastructure we need to build to support and enable the entire program.

"So, the board has a lot of opportunity to input as we are iterative in this reformation, and really bringing the whole cancer centers program up to a level of crisp clarity and impact."

GRAY: "I simply ought to make one more statement and that is to put out a plea that we get PIs to participate in the review process."

YOUNG: "This came up in the cancer center directors meeting, and many of us were thinking that we were the only ones that had--in writing--listed the names and phone numbers of all our senior leadership, volunteering them to participate in site visits, and to our collective discovery, hands went up all over the room. If you do the numbers, given the number of volunteers at that level, there ought to be somewhere around four to five members of senior leadership of cancer centers on each site visit review. Many of us have struggled to remember a single site visit in which a major leader was present. I don't know what's happened to all of those letters, but somehow, the volunteerism hasn't bubbled down in to the system the way one would hope."

WILLIAM HAIT, director, The Cancer Institute of New Jersey: "Having just come off the review committee recently, the review process is not quite what the guidelines outline. I think the etiology of the problem is in the vocal minority, the 30 percent of site visitors who are not involved in cancer centers in a direct way. I think the staff does a very good job of inculcating the parent committee in the guidelines and keep us on track, but that 30 percent, often superb young scientists who come in with a tremendous amount of energy for the site visit, and have a very clear R01-P01 basic science mindset. My suggestion might be that these people have an orientation before they go on a site visit, with a conference call to remind them that they should review the guidelines carefully, that the way the CCSG are reviewed are different from R01s and P01s. Perhaps that would calm them down a tad when they come loaded for bear to the site visit."

BSACHAIRMANFREDERICKAPPELBAUM, director, Clinical Research Division, Fred Hutchinson Cancer Research Center: "That is not a bad suggestion. It is true that there is something about the process of reviewing that you review what you can review. When you see tables with numbers, that's what you can see, rather than reviewing the somewhat more amorphous scientific accomplishments that grow out of this, so that's why I think people do tend to be bean counters sometimes."

Central IRB, Cooperative Group Participation

BSA member Richard Schilsky associate dean for clinical research, Biological Sciences Division, University of Chicago, and chairman, Cancer and Leukemia Group B, asked Antman whether cancer centers would be willing to take part in the NCI Central IRB.

"At least in our group, the academic centers, which are mostly cancer centers, contribute about 50 percent of the accrual to CALGB studies, so it would be great to see them embracing the Central IRB to a greater extent," he said.

About five centers make use of the Central IRB, said Michaele Christian, director of the NCI Cancer Therapy Evaluation Program. "We haven't gone to centers as a group to say are you interested in joining, but a number have joined and have used it repeatedly," she said.

"The other question deals with this whole issue of giving cancer centers credit for participating in cooperative groups," Schilsky said. "Credit is nice. Money is even better than credit. [Could] language be incorporated into the guidelines that would either provide incentives or recognize the opportunity for centers to provide core resources to support clinical trials conducted by the cooperative groups?"

NCI is studying that issue, in response to a recommendation of the Coalition of National Cancer Cooperative Groups, Antman said.

New Core for Dissemination

BSA member David Abrams, director, Brown University Center Behavioral and Preventive Medicine, said more formal incentives are needed for centers to support core resources for dissemination and behavioral science.

"The cross-cutting synergies that you get with a dissemination core would be not only recruitment and retention, reaching health disparity groups in clinical trials, which is critical, but you also get synergisms with improving adherence, follow-up, preventing missing data, doing things at the interface between community and population sampling and individual clinical trials," Abrams said. "It's not just bench to bedside that's so important. An equally critical transition is bench and bedside to dissemination into the community and the population."

ANTMAN: "Bench to trench."

ABRAMS: "Clearly, this is in line with transdisciplinary imperatives where the community is in fact the laboratory for certain kinds of basic research, and obviously what I mean by that is genetic epidemiology, where you need very large samples, or behavioral genetics, where you are interfacing or even combining molecular and genetic epidemiology. As we learn more about genes, we see how much low penetrance genes and multi-gene environment interactions require large samples.

"The laboratory for critical basic science research is the interface with populations and networks in the community. I'm wondering if that can be made a little more solid, formal, and articulated more explicitly as a transdisciplinary team criteria that ought to be in cancer centers, because that's where the biggest infrastructure is to pull off these very expensive, but very synergistic and perhaps efficient ways of moving science forward, both basic, clinical, and putting what's known into practice in the community."

ANTMAN: "Bob [Croyle, director, NCI Division of Cancer Control and Population Sciences] and Jon [Kerner, deputy director for research dissemination and diffusion, DCCPS] have inserted sections into the revised guidelines and have inserted 'transdisciplinary' almost everywhere they could."

CROYLE: "It's mostly opening up how people can use cores for centers and the mission they fulfill, and changes the criteria in terms of usage, and how they are used by individual investigators, so that the bang for the buck is not just the number of people using sample tissue collections, but in the case of larger scale or ambitious gene-environment interaction studies, there may be actually fewer investigators using a core, but the core might have much more constant leverage in terms of efficiency, than, for example, a survey research core. We have been trying to work through those problems with Karen and the program to try to make sure the language is flexible, so that people could maximize resources in a cancer center to accomplish multiple goals including dissemination."

DAVID ALBERTS, director, cancer prevention and control, Arizona Cancer Center: "We just went through renewal, so now I have to wait another five years for dissemination. I think that's one of the most important issues in cancer prevention and control, and I would like to put out the possibility that there might be supplements to develop this. Because it's almost impossible to do it unless there is some funding, to do it in a consistent way."

ANTMAN: "We can certainly consider it, although this year it's unlikely to happen."

SHELTON EARP, director UNC Lineberger Comprehensive Cancer Center: "There are two areas

of research which have traditionally been under-funded and that is clinical research and population sciences. Most of our basic sciences do well and their cores have an algorithm that's easy to review. Clinical research used to be funded by excess clinical revenue. All of you remember those days, but they are gone. Therefore, the working group put a couple things in there, the clinical investigator probably being the one that got a 100 percent vote, and more money for regulatory, tissue banks, clinical trials core. It was realized that, yes, you could have those now, but there is kind of a cap on it, because you have to put all of this together. If you look at the cancer center as a gravitational force, then we are going to need to put more of that into cancer centers over time. The clinical investigator category is probably the most important. We all worry about how to keep those people funded.

"Moving to population sciences, there actually is a reason why it was split into two parts, 2.4 and 2.6. 2.6 is about cores for population sciences. We need to get away from the exact analogy to the high through-put basic science cores, because the number of R01 funded research projects in this area is fewer. So you have to have criteria which are not just a process, but reward building a community of scholars. These cancer center cores are going to have to be considered like a structural biology core. There are a small number of people who will use them, but they are going to make important contributions.

"2.4 was about staff to build relationships that are needed if we believe cancer centers are going to be the organ by which NCI relates to the population in a region through the state health departments, the CDC and ACS. It's more than a budget for an associate director for outreach or cancer control. If you really want to understand what's going on in your state and have an impact, you need a staff to put a structure in place so that agencies know that the centers are there to help—to implement changes that all agree upon. In some ways it is the most radical thing in that report, because it's infrastructure for dissemination and for research, but you are never going to be able to say that this R01 got funded by this part of the budget--it's a stretch. The accomplishments won't be buttressed by R01 funding, but it's crucial to the ability of cancer centers to look out to the states. It will require a different set of guidelines."

ANTMAN: "We put that in the administrative section. Can you think of a better way?"

EARP: "That's a very reasonable place to put it."

ABRAMS: "The issue of setting up outreach infrastructure and synergizing with state cancer plans is a critical issue; however, I think you can also expect that once you put that infrastructure in place, which can sometimes take years to develop the networks and solid resources with the community, it becomes a rich opportunity for research. You can piggyback R01s in prevention and control and get a much bigger volume by setting up that laboratory infrastructure, and research could involve things like: how do you disseminate and improve networks of dissemination; research on how do you reach underserved and health disparity populations with evidence-based state-of-the-art treatment that may be delivered in an academic cancer center but is not being delivered in the rest of the state. I think there are now examples of that, where research is looking at ways to efficiently disseminate. You can piggyback the research on the service and the outreach programs, not just an outreach program in the way that CDC or a state may have an outreach program."

Budgets: Centers, R01s, Subcontracts

BSA member Hedvig Hricak, chairman of the department of radiology, Memorial Sloan-Kettering Cancer Center, said she hoped the emphasis on the cancer centers would not detract from NCI's funding for R01s. "My concern is how can we make sure we balance the money for R01s, because I think our most innovative research still comes from the R01," Hricak said. "I always feel that cancer centers have advocacy groups, and R01s are just there by themselves, and how can we assure that there is balanced and sufficient funding?"

"I think the track record this year speaks for itself," von Eschenbach said. "We put the R01 20 percent payline as the No. 1 priority from which everything else flowed. We recognize that there are a whole list of important and competing priorities that make up this portfolio, and balancing the portfolio is always what's going to drive the investments from a philosophical point of view. But it's also going to be the quality and the impact of the programs.

"I think in this particular conversation what we are talking about is how do we nurture this program specifically because of the incredible leverage opportunity that it has and how we can significantly enhance all of the rest of the things that we are talking about in the portfolio," von Eschenbach said. "It's not to disadvantage another program."

"A lot of money for the centers goes into cores that make those R01s much more efficient," Antman said.

BSA member Hoda Anton-Culver, chief of the epidemiology division, University of California, Irvine, said cancer centers don't get credit for subcontracts that come through the university, and not directly to the center.

Cancer Centers Branch Chief Linda Weiss said the NCI base is calculated in a standardized way and presented to the parent committee at the time of review. "Those numbers are generated from the Research Analysis and Evaluation Branch here at NCI, and we generate for all institutions competing in the same fiscal year, at the same time, so we get standard information across the board for all competitors," Weiss said. "You are correct that subcontracts are not included, because RAEB draws its data from the data that are actually going directly to that institution in terms of grant support.

"You do have the opportunity to present those at the time of the site visit," Weiss said. "I think in instances where it is very well justified, reviewers have been reasonable in taking those additional dollars into account as they calculate the final award."

ANTON-CULVER: "Is there any way we could have that as a separate category in the table we have to provide?"

WEISS: "I don't know that there is any way that we can draw those data ourselves from NCI. We could investigate that. But one advantage of using the database RAEB provides, is that it is unquestionable in terms of the NCI grants going directly to the institution and it provides a very clean kind of database across the board for all centers. Once we start bringing in information from other kinds of sources that are batched together, it becomes more difficult to know that we are doing this in a standard way."

ANTMAN: "At least it's fair for everybody, and its verifiable."

In Brief:

NCCS, Wellness Community, Begin Advocacy Initiative

(Continued from page 1)

M. D. Anderson's Mexican-American Cohort Study, which is looking at social, genetic and environmental factors in cancer susceptibility. . . . **NATIONAL COALITION for Cancer Survivorship** and The Wellness Community have begun Cancer Advocacy Now, a grassroots advocacy initiative. The network, composed of cancer survivors and others, will work to affect change at the federal level on the delivery and payment for quality cancer care. "It's no coincidence that NCCS' first partner in this new project is The Wellness Community," said **Ellen Stovall**, president and CEO of NCCS. "In a sense, we've gone back to our roots in peer support—Dr. Harold Benjamin, who founded The Wellness Community, is one of NCCS' founders, too. NCCS hopes that other organizations committed to quality cancer care will join as future partners in this outreach and education." NCCS Director of Grassroots Advocacy **Robin Atlas** will oversee the program at NCCS. Participants will receive email updates on policy issues and advocacy training focused on cancer care and treatment. The first of the in-person advocacy training sessions planned for The Wellness Community locations take place in late April and May in Philadelphia, Wilmington, and Sarasota. Information is available at www.canceradvocacynow.org. . . . **NATIONAL PATIENT ADVOCATE FOUNDATION** has begun AccessWatch (www.AccessWatch.org), a new Web site created with support from US Oncology, to monitor the impact of the Medical Modernization Act of 2003 on community cancer care. The site invites cancer patients, family members, care givers, and others to document and describe the impact of the new law. AccessWatch plans to track and analyze information including treatment site closures; diminished access of Medicare beneficiaries to cancer caregivers; delays in treatment and increased costs associated with the referral of patients from the community setting to hospitals; a reduction in community cancer practice clinical research capacity; a reduction of Medicare beneficiaries' access to the latest, most effective therapies; and reductions of cancer care practice capacity to absorb charity care. **Nancy Davenport-Ennis** is president and CEO of NPAF. . . . **CANCER RESEARCH and Prevention Foundation** honored seven individuals for their work in colorectal cancer research and prevention. They were: **Nathaniel Cobb**, director of cancer prevention and control, Indian Health Service; **Amelie Ramirez**, associate professor of medicine and deputy director of the Chronic Disease Prevention and Control Research Center, Baylor College of Medicine; **Robert Smith,** director of cancer screening, American Cancer Society; **Cindy Iverson**, development director for the Minnesota Colon and Rectal Foundation; **Meinhard Classen,** president of the World Organization of Gastroenterology; **Paul Rozen,** chairman of the World Organization for Digestive Endoscopy and professor of medicine at Tel Aviv University; **Sydney Winawer**, the Paul Sherlock Chair at Sloan-Kettering Cancer Center, co-chairman of the International Digestive Cancer Alliance.

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Business & Regulatory Report

Deals & Collaborations:

ImClone Receives $250 Million Payment From Bristol-Myers For Erbitux Approval

ImClone Systems Inc. (Nasdaq: IMCL) of New York said it has received a $250 million milestone payment under a license agreement with **Bristol-Myers Squibb**.

The cash payment was triggered by FDA approval of Erbitux for irinotecan refractory or intolerant metastatic EGFR-expressing colorectal

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Oncology Management:

NCCN Releases Report on GIST Treatment, Updates Practice Guidelines For NSCLC

National Comprehensive Cancer Network of Jenkintown, Penn., released the NCCN Gastrointestinal Stromal Tumors Task Force Report, an expansion on the NCCN Sarcoma Clinical Practice Guidelines in Oncology. Also, the group has updated its Non-Small Cell Lung Cancer Clinical Practice Guidelines.

GIST is increasingly recognized after experts reported that imatinib, (Gleevec, Novartis Pharmaceuticals) an oral cancer therapy which targets a molecular switch important to the tumor cells, could induce dramatic remissions and prolong survival for patients with advanced GIST.

"The clinical care of patients with GIST has changed radically in the past few years thanks to the rapid evolution of research translating into new and effective therapeutic strategies," said George Demetri, chairman, GIST Task Force and director of the Center for Sarcoma and Bone Oncology at Dana-Farber Cancer Institute. "The report represents the work of expert physicians from several disciplines, such as pathology, surgery, medical oncology, and radiology. Together, we have outlined the most effective approach for optimal management of GIST patients. Our aim is to increase awareness of the tremendous changes which have developed in such a short time in our approach to patients with GIST, and to identify opportunities for future research to improve outcomes further."

The task force report describes the cooperative multidisciplinary effort among medical oncology, surgery, pathology, and other specialties that is necessary to achieve the best possible results, which include reducing the incidence and risks of recurrent disease, optimizing disease control, improving quality of life by minimizing surgery that might impair function, and prolonging survival, the network said.

NCCN updated the non-small cell lung cancer guidelines to include

(Continued to page 6)

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ImClone Reaches Milestone; Genzyme, ILEX Plan Merger

(Continued from page 1)

cancer in February of this year.

"This milestone payment represents the acknowledgement by Bristol-Myers Squibb of the progress that we have made together in the Erbitux clinical program, which culminated in the recent approval of the drug in combination with irinotecan and as a single agent in certain patients with late-stage colorectal cancer," said Daniel. Lynch, CEO of ImClone Systems. "The company is dedicated to working closely with its partners Bristol-Myers Squibb and Merck KGaA to conduct additional clinical trials to expand the potential application of Erbitux in colorectal and other EGFR-expressing cancers."

* * *

Genzyme Corp. (Nasdaq: GENZ) and **ILEX Oncology Inc.** (Nasdaq: ILXO) announced a merger agreement under which ILEX shareholders will receive shares of Genzyme common stock valued at $26.00 per share, or approximately $1 billion in equity value.

Excluding amortization, the transaction is expected to be dilutive to Genzyme's near-term earnings and accretive in 2006.

The Ilex pipeline significantly augments Genzyme's program in oncology, which includes a research and early development portfolio with particular strengths in antibodies, small molecules and cell-based therapeutics, the companies said. The merger also capitalizes on Genzyme's expertise in biologics and targeted therapeutics, and its oncology testing business.

"This transaction is a very good strategic fit for Genzyme that provides us with a solid franchise in the important field of oncology," stated Henri Termeer, Genzyme chairman and CEO. "Through this merger, we gain an experienced team that has brought a cancer therapy from development to market. The combined strength of the ILEX program and Genzyme's oncology pipeline expertise and infrastructure will provide the foundation for a sustainable and competitive commercial oncology business."

Genzyme plans to maintain ILEX operations in San Antonio, acknowledging the impressive work currently underway by the ILEX team.

"We believe this transaction brings significant value to ILEX shareholders and recognizes the high quality oncology franchise that we at ILEX have built," said Jeffrey Buchalter, ILEX president and CEO. "Genzyme is a top-tier biotech company with the resources and commitment to take us to the next level as we continue to expand our markets and, ultimately, commercialize our own products."

ILEX's lead product, Campath (alemtuzumab for injection), is indicated in the United States for the treatment of B-cell chronic lymphocytic leukemia. Campath is a humanized monoclonal antibody that binds to a specific target, CD52, on cell surfaces directing the body's immune system to destroy malignant cells.

FDA approved Campath for B-CLL in patients who have been treated with alkylating agents and who have failed fludarabine therapy. ILEX and marketing partner, Schering AG (NYSE: SHR), are conducting additional trials with the agent.

ILEX's lead pipeline candidate is clofarabine, a next-generation purine nucleoside analogue that inhibits both DNA and RNA synthesis. ILEX is currently investigating clofarabine for use in pediatric and adult acute leukemias, as well as advanced solid tumors. ILEX has initiated a rolling NDA with FDA for treatment of relapsed or refractory acute leukemias in children following receipt of a fast track designation, and Genzyme expects approval of clofarabine in 2005. Also, ILEX holds the rights from Bioenvision, Inc. (Amex: BIV) to develop and market clofarabine for cancer applications in the United

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States and Canada. Bioenvision is responsible for developing clofarabine in the rest of the world.

ILEX's phase II pipeline candidate is ILX-651, a synthetic analog of the natural substance dolastatin that has a unique mechanism of action targeting tubulin. ILEX is currently enrolling Phase II trials in melanoma and non- small cell lung cancer after seeing promising activity in Phase I solid tumor trials. ILEX has exclusive worldwide rights to ILX-651 in cancer.

Genzyme's business combination with ILEX will take the form of a stock- for-stock merger and is expected to be completed by the middle of the year, the companies said. ILEX shareholders will receive shares of Genzyme General common stock for each ILEX share owned based on an exchange ratio. This exchange ratio will equal $26.00 divided by the average (rounded to the nearest cent) of the per share closing prices of Genzyme common stock as reported by Nasdaq during the 20 trading days ending on the fifth trading day prior to the closing of the transaction, provided that if this average is greater than $59.88, then the exchange ratio will be 0.4342, and if this average is less than $46.58, then the exchange ratio will be 0.5582. Cash will be paid for fractional shares.

The tax-free transaction has a total value of approximately $1 billion, based on ILEX's 39.0 million shares outstanding today and Genzyme's offer price of $26 per share.

In another development, Genzyme and Impath Inc. (OTC: INPHQ.PK) said they have entered into a definitive agreement under which Genzyme will become the lead bidder to purchase the assets of the Impath Inc. Physician Services business unit.

Under the agreement, Genzyme will purchase the unit for approximately $215 million in cash, and combine it with the Genzyme Genetics business unit, the company said.

Impath Inc. filed for Chapter 11 bankruptcy protection in September 2003, the company said. The Physician Services will proceed through a competitive auction process, pursuant to Section 363 of the Bankruptcy Code. The definitive agreement, subject to Bankruptcy Court approval, gives Genzyme certain right, including a break-up fee should the assets be sold to another party through the auction, the company said.

Sale of the assets will be completed in the second quarter of 2004, the company said.

Through the acquisition, Genzyme would obtain oncology diagnostics in solid-tumor and blood-based cancers, testing laboratories in New York, Phoenix and Los Angeles, and a team of board-certified anatomic and clinical pathologists with experience in oncology testing, the company said.

Genzyme said it plans to maintain operations at the Impath facilities and hire all of Impath Physician Services employees.

* * *

Biobase of Martinsried, Germany, said it has signed a license agreement with **GPC Biotech AG** (FSE: GPC; TecDAX 30) for Transpath, a signal transduction database.

An in-house developed product of Biobase, the database contains information on human and mammalian cells, the company said.

The scientific standard of the database is based on the manual annotation of primary literature by molecular biologists, an advantage for cancer research and drug development when compared to automatically extracted data, the company said.

The system can be used as an encyclopedia, for general or specific information about signal transduction, for analysis of biological networks and gene expression data, as well as for searching for target molecules of new agents, the company said. In addition to the extracted data from literature, the database contains the following tools: PathwayBuilder, for the visualization of networks, and ArrayAnalyzer, for interpretation of gene expression arrays and for identification of key molecules in signal networks as possible targets.

* * *

Children's Memorial Institute for Education and Research of Chicago and **The Translational Genomics Research Institute** of Phoenix, Ariz., said they have formed a partnership to conduct genomic research into childhood illnesses and their relationship to adult diseases.

The two institutes will conduct research on problems, including cancer, brain disorders such as schizophrenia, behavioral disorders, autism, multiple sclerosis, developmental defects, and autoimmune diseases, said Mary Hendrix, president and scientific director of the Children's Memorial Institute for Education and Research, and professor of pediatrics at Feinberg School of Medicine, Northwestern University.

* * *

Chiron Corp. (Nasdaq: CHIR) of Emeryville, Calif., and **Xoma Ltd**. (Nasdaq: XOMA) of Berkeley, Calif., said they have entered into a worldwide,

exclusive, multi-product, collaborative agreement to develop and commercialize antibody products for cancer.

Under the agreement, the companies said they would jointly research, develop, and commercialize multiple antibody product candidates.

"Our collaboration represents significant growth in our product pipeline in the cancer arena and also demonstrates the value of the work Xoma has done in building multiple capabilities and experience in biopharmaceutical development, especially in the monoclonal antibody field," said John Castello, president, chairman and CEO of XOMA. "The collaboration takes advantage of capabilities that we've built up, ranging from phage display and our proprietary Human Engineering technologies, through process development and manufacturing scale-up, to preclinical, clinical and regulatory capabilities."

* * *

Corixa Corp. (Nasdaq: CRXA) of Seattle and **GlaxoSmithKline** (NYSE: GSK) and **Biogen Idec** said they have reached a settlement with on patent litigation.

Under the settlement, Biogen Idec will Corixa and GSK a $20 million upfront settlement payment, as well as a one-time milestone payment based on future Zevalin sales performance, and royalty payments on Zevalin sales from January 1, 2004 until all Bexxar patents expire, the companies said. Corixa and GSK will also enter into a worldwide, cross-license agreement with Biogen Idec relating to patents in suit.

* * *

Helsinn Healthcare SA of Lugano, Switzerland, and Taiho Pharmaceutical Co. Ltd. of Tokyo said they have entered into an exclusive license and distribution agreement under which Taiho acquires the rights to develop and commercialize palonosetron in Japan for nausea and vomiting resulting from chemotherapy.

In the U.S., the agent is marketed under the trade name Aloxi by MGI Pharma for acute or delayed nausea and vomiting associated with initial and repeat courses of moderately and highly emetogenic cancer chemotherapy, the company said. The product is under regulatory review in Europe where it will be marketed by Italfarmaco in Italy and Spain under the trade name Onicit. In Korea the product shall be marketed by CJ Corp.

Palonosetron hydrochloride is a selective 5-HT3 receptor antagonist with binding affinity and an extended plasma half-life of approximately 40 hours, the company said. Results from phase III trials demonstrate that a single intravenous dose of palonosetron is effective in preventing both acute and delayed CINV in patients receiving moderately emetogenic chemotherapy. Palonosetron is the only 5-HT3 receptor antagonist to be approved for this indication by FDA, the company said.

* * *

Hudson Health Sciences Inc. of South San Francisco said it has licensed IPdR, a radiosensitizer, from **Yale University** and **The Research Foundation of the State University of New York**.

IPdR is being developed as a radiation sensitizer for brain cancers.

IPdR is an orally available, halogenated dThd analogue and prodrug for IUdR, an intravenous tumor radiation sensitizer, the company said. Data from preclinical studies concluded that IPdR is a superior radiosensitizer compared to IUdR in terms of safety and efficacy with a lower toxicity profile, including gastrointestinal and hematological side effects.

"IPdR can significantly advance the field of radiosensitizers," said Yung-Chi Cheng, Henry Bronson Professor of Pharmacology at Yale University and co-inventor of the technology in conjunction with researchers at the University at Buffalo. "Radiosensitizers are already being investigated in cancers with brain metastases and have had promising results thus far. IPdR could be an important treatment option."

* * *

Merix Bioscience said it has signed a joint licensing agreement with **Geron Corp**. to develop cancer vaccines.

Clinical testing utilizing the combined technologies is ongoing at Duke University Medical Center, the company said.

In exchange for five million shares of Geron stock, valued at $43 million, Merix will allow Geron to use its platform technology for modifying dendritic cells to present one or more defined antigens to provoke an anti-tumor immune response, the company said. Merix retains co-exclusive rights to use the platform technology with defined antigens other than the Geron telomerase antigen and exclusive rights to use it with total tumor RNA and other uncharacterized antigens.

"The validation of our technology in several clinical trials at Duke, including the ongoing trial which combines the Merix antigen delivery technology with

the telomerase antigen, is especially encouraging as we begin our initial corporate clinical trial using total tumor RNA in metastatic renal cell carcinoma in North America," said Clint Dederick, Jr., chairman and CEO of Merix. "We believe that utilizing all of the patient's tumor antigens, i.e., total tumor RNA, has the advantage of inducing the broadest possible immune response, maximizing the chance of effective anti-tumor responses."

The technology involves extracting RNA from a tumor, combining it with dendritic cells from the patient, and reintroducing the now personalized vaccine back into the patient, the company said. This stimulates the immune system to recognize and fight the specific cancer residing within the body.

* * *

Maxim Pharmaceuticals (Nasdaq: MAXM) and **Shire BioChem Inc.** entered into an agreement with under which Maxim has reacquired the rights to the MX2105 series of vascular targeting agent cancer drug candidates, the companies said.

The MX2105 series was licensed in 2000 to BioChem Pharma, a company that was subsequently acquired by Shire Pharmaceuticals. Last year, Shire Pharmaceuticals announced that it was exiting oncology research.

MX2105 was identified through Maxim's high-throughput caspase-based screening assay. In conjunction with the license, Maxim and Shire BioChem collaborated on the development of the MX2105 family under a joint research agreement. As part of these efforts, Maxim's chemistry group designed and synthesized over 300 analogs within the MX2105 family to determine the structure-activity relationship and to improve pharmacological properties.

Compounds within the MX2105 series have been tested in multiple tumor xenograft models and have demonstrated activity against multiple cancer types, including breast cancer, lung cancer and colorectal cancer, the company said.

The new agreement calls for Maxim to pay Shire BioChem certain milestone and royalty payments upon the successful advancement of any drug candidates within the MX2105 series.

U.S. and international patents and patent applications encompass the composition of matter and use of MX116407 and other analogs within the MX2105 series, the company said. The MX2105 series is one of more than 40 compound families identified by Maxim through its proprietary caspase-based high-throughput screening system that targets the identification of compounds that modulate programmed cell death, or apoptosis.

Maxim said two abstracts describing the results of preclinical testing of compounds within the MX2105 series have been accepted for presentation at the American Association for Cancer Research Annual Meeting to be held March 27-31.

* * *

Misonix Inc. (Nasdaq: MSON) said it has signed an exclusive distribution agreement with **Focus Surgery Inc**. for the sale of the Sonoblate 500 for prostate cancer, enlarged prostate and other prostatic tumors in Western Europe, Eastern Europe and Russia.

The agreement is for a term of two years with a provision for automatic renewals for successive one-year terms as long as the minimum quantities are purchased, the company said.

The device, which uses high frequency focused ultrasound, has a CE mark and has treated more than 90 patients in Germany with clinical applications throughout Europe, the company said.

The device is being evaluated in 40 patient phase I study in the U.S., the company said. Twenty-four of the patients have been treated successfully with the remainder to be treated.

* * *

Spectral Genomics Inc. of Houston said it has entered into a worldwide licensing agreement with **Affymetrix** that provides Spectral with Affymetrix patents to manufacture and sell spotted DNA arrays in the diagnostic market.

The license supports the SG constitutional chip, which would be introduced in 2004, as well as specialty arrays for cancer diagnostics, the company said. While selling the chips as research products, SG said it is seeking regulatory approval for the products as diagnostics.

"The license allows us to seek approval of diagnostic products that will have significant impact on the future of pre- and post-natal and cancer diagnostics," said Edward Chait, CEO of Spectral Genomics.

The company said it develops and manufactures BAC clone arrays that can cover the entire genome representing all the chromosomes at ten times higher resolution than with traditional cytogenetic techniques. The arrays are used in research in pre-natal and post-natal genetic defects and in cancer research.

Oncology Management:

NCCN Updates Guidelines For GIST And Lung Cancer

(Continued from page 1)

gefitinib (Iressa, AstraZeneca Pharmaceuticals LP) as a recommended third-line therapy and as second-line only if the platinum/docetaxel combination was used as first-line therapy, the network said.

The guidelines panel has added greater detail to its recommendations for administration of chemotherapy, including patient selection criteria and definition of first, second-, and third-line agents and combinations, the network said.

Chemotherapeutic agents are specified as two-agent regimens for first-line therapy, two agent regimens or single agents for second-line therapy, and one single agent for third-line therapy.

Agents used in first- and second-line therapy are: cisplatin (Platinol, Bristol-Myers Squibb Co.), carboplatin (Paraplatin, Bristol-Myers Squibb Co.), paclitaxel (Taxol, Bristol-Myers Squibb Co.), docetaxel (Taxotere, Aventis Pharmaceuticals Inc.), vinorelbine (Navelbine, GlaxoSmithKline), gemcitabine (Gemzar, Eli Lilly and Co.), etoposide (Toposar, Pfizer Inc.; VePesid, Bristol-Myers Squibb Co.; Etopophos, Bristol-Myers Squibb Co.), irinotecan (Camptosar, Pfizer Inc.), vinblastine (Velban, Eli Lilly and Co.), mitomycin (Mutamycin, Bristol-Myers Squibb Co.), and ifosfamide (Ifex, Bristol-Myers Squibb Co.).

NCCN Clinical Practice Guidelines in Oncology and other publications can be ordered from NCCN by phone 215-690-0300 or at the Web site at www.nccn.org.

In another development, NCCN and the **American Cancer Society** said they have created the Bladder Cancer Treatment Guidelines for patients.

The NCCN guidelines are derived directly from the Clinical Practice Guidelines in Oncology developed for physicians by NCCN experts, the groups said. The patient guidelines also provide background information on different types of cancers, their causes, various treatment options, and a glossary of terms.

* * *

ASI Business Solutions Inc. of King of Prussia, Penn., said it has been selected by **American Pharmaceutical Partners Inc**. (Nasdaq: APPX) to provide their Abraxis Oncology sales group with a business performance management system.

Some of the system components included the ASI Reward, the ASI solutions for sales force automation; ASI Inquire, for business intelligence, knowledge management (e-PharmaToday); ASI Compensation Assistant, for incentive compensation, and ASI Realignment Manage, for territory realignment, the company said.

ASI said it would provide APP with a set of support services including systems hosting, help desk, technical and operations support.

* * *

University of Pittsburgh Cancer Institute selected **ImmunoSite** to monitor patients on clinical trials of immuno-potentiator drugs.

"ImmunoSite provides UPCI with a tremendous opportunity to quickly and cost effectively understand the influence of vaccines, small molecules or other promising drugs in modulating the patient's immune system to combat cancer or other diseases," said Ronald Herberman, director of UPCI. "This service could save the pharmaceutical industry millions of dollars in clinical trial costs that result from insufficient understanding of these interactions, and to more quickly develop life-saving treatments for disease."

ImmunoSite's services will provide efficacy data of immunopotentiating drugs in oncology, inflammation, autoimmunity, infectious diseases, immunotoxicology and organ transplant rejection, the institute said. The information would provide insights into the mechanisms of action of the drug, dosing regimens and biological activities, yielding data to support decision-making through all phases of clinical trials.

* * *

Varian Medical Systems Inc. (NYSE: VAR) of Palo Alto, Calif., said it has entered into an agreement to acquire the assets of **OpTx Corp.** of Denver.

The acquisition enables Varian to offer an integrated single software system for managing and coordinating radiation therapy and chemotherapy routinely used for cancer treatment, the company said.

Varian will pay $18 million to acquire the OpTx assets, including the OpTxTools software, which it will continue to develop, sell, install, and service worldwide as a stand-alone product for medical oncology practices and as part of its VARiS software for coordination with radiation oncology.

Varian said it has been selling the OpTx software as VARiS MedOncology under a private label agreement with OpTx since 2001.

The software enables cancer treatment facilities to document patient data, manage clinical trials, track complex drug interactions, administer prescriptions, and schedule treatments for chemotherapy, the company said.

Varian said the acquisition would add annualized revenues of $9 million and be nearly neutral to earnings in the current fiscal year.

* * *

Webridge Inc. of Portland, Ore., said the **University of Michigan** began a campaign that will use its Webridge Compliance Extranet to automate submission and processing of research projects.

To help investigators and review committees keep pace with the rising volume and the complexity of federal regulations, while protecting study participants, the UM began the Michigan Program for Research Information Management and Education project. Over the next year, the MPRIME project will use Webridge Compliance Extranet to streamline the human research submission, review, and approval processes. All the Institutional Review Boards and other human research compliance committees will participate, including the IRB of the Medical School, the IRB for Behavioral Science, the IRB for Health, and the IRBs at the Flint and Dearborn campuses, the company said. The General Clinical Research Center and the Protocol Review Committee/Cancer Center will also participate.

Using Webridge SmartForms, research investigators will be guided through a single institutional online application process that incorporates the requirements of the various compliance committees, the company said.

"With the new system, we expect to accommodate the growing volume and complexity of human research while reducing the approval cycle time of research applications through the compliance committees," said Marvin Parnes, associate vice president for research.

The MPRIME is partially funded by NIH, the university said. The Human Research module would be available to researchers late in 2004.

Clinical Trials:

DSMB Advises Continuation Of Phase III Canvaxin Trial

CancerVax Corp. (Nasdaq: CNVX) of Carlsbad, Calif., said an independent data and safety monitoring board recommended the continuation of its randomized, double-blind, international phase III trial of the investigational immunotherapy, Canvaxin, for stage III melanoma.

The DSMB said clinical endpoints can be met to establish the effectiveness of the agent, and that no unexpected or serious toxicities prevent the continuation of the study, the company said.

The DSMB also recommended the continuation of another phase III trial of investigational immunotherapy for stage IV melanoma.

The clinical data remains blinded to the company, CancerVax said. As a result, the trial will remain intact to serve as a study for the submission of a biologics license application of the immunotherapy for advanced-stage melanoma.

The interim analysis was conducted on data from 842 patients, the company said. CancerVax said it expects enrollment to be completed for stage III melanoma this year.

In another development, CancerVax Corp. said it has obtained an exclusive, worldwide sublicense from **SemaCo Inc.** of Delaware to develop technology using telomere homolog oligonucleotides, or T-oligos, for cancer.

Preclinical studies in murine models of photocarcinogenesis suggest that T-oligos may activate defense mechanisms used by healthy cells to prevent malignant transformation, the company said. Other data show T-oligos may cause apoptosisof cultured human melanoma and lymphoma cells.

Under the sublicense agreement, SemaCo will receive an upfront license fee and patent cost reimbursement, research support, payments for regulatory and other milestones, and royalties upon commercial sales, the company said.

* * *

Point Therapeutics Inc. (OTCBB: POTP) of Boston said it began a phase II trial of PT-100 in advanced non-small cell lung cancer.

The study will evaluate the anti-tumor and hematopoietic activity of the compound in combination with Taxotere for stage IIIb/IV NSCLC patients.

Forty-one patients will be studied in the single-arm, two-stage study evaluating the overall tumor response rates for advanced NSCLC where a platinum-containing regimen as first-line treatment has failed, the company said. At mid-point, tumor response rates will be compared to historical response rates to evaluate trial continuation. Other secondary endpoints will also be evaluated, including duration of tumor response, time to disease progression and

incidence of severe neutropenia and anemia.

"Our clinical plans are to study PT-100 in three clinical indications and in combination with two different chemotherapeutic agents, a monoclonal antibody and as a single-agent therapy," said Don Kiepert, president and CEO of Point Therapeutics. "We have demonstrated that PT-100 stimulates a variety of cytokines and chemokines which provide upregulation of both innate and acquired immune systems. Because of PT-100's activity, we believe PT-100 can be developed as both an anti-tumor agent and hematopoietic stimulant."

The company said it plans to conduct other phase II studies, including PT-100 in combination with cisplatin for metastatic melanoma, PT-100 in combination with Rituxan for chronic lymphocytic leukemia, and a study of single-agent PT-100 in metastatic melanoma.

Product Approvals & Applications:

FDA Plans Steps To Spur Availability Of Generic Drugs

FDA said it would provide information for generic drug applicants to determine whether they are eligible for 180 days of marketing exclusivity, an incentive that helps get generic drugs to market sooner.

The period of marketing exclusivity is provided to the first generic drug that challenges a patent for the innovator product, FDA said. The marketing exclusivity motivates generic drug development provided under the Hatch-Waxman Amendments to the Federal Food Drug and Cosmetic Act. FDA also said it would implement the major reforms in the Hatch-Waxman law contained in the Medicare Modernization Act of December 2003.

'The steps we are announcing today will further spur the development and availability of generic drugs, which are an increasingly important way to provide the American people with safe, effective and affordable medical treatment," said FDA Commissioner Mark McClellan. "We have the most competitive generic drug industry in the world with some of the lowest generic drug prices in the world, and we intend to enhance it to help consumers."

In response to two citizen petitions, FDA will now disclose on its Web site the date on which the first complete generic drug application containing a challenge to a patent listed for the innovator drug was submitted to the agency.

By displaying the submission date along with the trade and generic name of the drug, its dosage form, and the strengths of the drug products, the agency said it will provide a fairer, more transparent way for all interested parties to gain access to this information.

It is important to note, however, that FDA said it would continue its policy of not disclosing the identity of the firm making the submission.

In addition, the agency will publish a Federal Register notice seeking public comment on how best to implement reforms to the Hatch-Waxman Amendments that were outlined in the recently enacted Medicare Law. The reforms are designed to clarify the conditions under which 180-day marketing exclusivity can be given. The Medicare Law also established a limit on how long approval of generic drugs can be delayed while patent rights are being litigated in court.

FDA is requesting public comment within 60 days, so the agency can implement the legislative reforms that speed the approval of generics. The agency will also issue a Federal Register notice revoking a regulation the agency had issued last year that limited how long approval of a generic drug can be delayed while patent rights are litigated in court.

FDA said it plans to post generic drug application dates at www.fda.gov/cder/ogd/ppiv.htm.

* * *

American Pharmaceutical Partners Inc. of Schaumburg, Ill., and **American BioScience Inc.** said ABI has completed the filing of an NDA for Abraxane for metastatic breast cancer.

Abraxane is the first solvent-free nanoparticle albumin-bound chemotherapeutic, and that may exploit an inherent pathway for albumin receptor-mediated transport of drugs across endothelial cell walls of tumor neovasculature, the companies said.

The NDA was submitted under the FDA Fast-Track designation with a request for priority review designation, the companies said.

The filing of the NDA is based upon supportive phase I and II clinical trials a randomized controlled phase III trial that compared the safety and efficacy of 260 mg/m2 of Abraxane to 175 mg/m2 of Taxol administered every three weeks in 460 patients, the companies said. In the phase III trial, the drug resulted in a doubling of the response rate and a prolongation of time to tumor progression in first and second line patients. In addition, the study confirmed the agent could be administered safely over 30 minutes without the need for steroid premedication.

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