THE CANCER LETTER

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# A Tissue Bank To Break The Bank? NCI, Dialogue Plan Expensive Resource

The National Dialogue on Cancer and the National Cancer Institute are developing a plan to take tumor tissue banking outside the Institute and place it under control of a not-for-profit organization.

Documents obtained by **The Cancer Letter** demonstrate that the proposed "National Biospecimen Network" would collect tissue from cancer patients not enrolled in clinical trials and develop an informatics system for life-long follow-up of the donors.

Today, the most significant tissue banks are operated by the NCI-

(Continued to page 2)

*In Brief:*

## Weber Returns To M.D. Anderson To Direct Head & Neck Surgery; Becker Exhibit Opens

**RANDAL WEBER** was named head of the Dept. of Head and Neck Surgery at The University of Texas M. D. Anderson Cancer Center. Weber, who spent his early career at M.D. Anderson, returned after seven years as vice chairman, Dept. of Otorhinolaryngology-Head and Neck Surgery and director, Center for Head and Neck Cancer, Hospital of the University of Pennsylvania. **Helmuth Goepfert**, former chairman of the department, retired last month. . . . **FREDERICK BECKER** is being honored with a permanent exhibit of memorabilia that reflects his 27-year career at M. D. Anderson. Before retiring in 2001, Becker was special advisor to **John Mendelsohn**, president of MDACC. . . . **WINSHIP CANCER INSTITUTE** of Emory University made two staff appointments. **Ruth O'Regan,** assistant professor of medicine, Northwestern Hospital, was named director of the Translational Breast Cancer Research Program and assistant professor of hematology and oncology. **Nabil Saba**, director of cancer research and assistant professor of medicine at University of Minnesota, was appointed assistant professor of hematology and oncology and director of house staff education programs. . . . **ANTHONY SHIELDS** was appointed associate director for clinical research at Barbara Ann Karmanos Cancer Institute. Shields is leader of the gastrointestinal oncology multidisciplinary team, program leader for developmental therapeutics, and professor of medicine and oncology at the institute. . . . **ANDREW TURRISI** was named chairman and chief of radiation oncology in the Dept. of Radiation Oncology at Wayne State University School of Medicine. Turrisi is professor and chairman, Dept. of Radiation Oncology, Medical University of South Carolina, and principal investigator for the Southwest Oncology Group.



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## Cancer Dialogue, NCI Plan A "Space Station" Of Tissue

(Continued from page 1)

funded clinical trials cooperative groups, which have the capability to correlate any piece of tissue with the treatments and outcomes for each patient over the duration of a trial.

There is no debate that researchers need increasing amounts of tumor tissue for studies of cancer on the molecular level. While basic scientists need tissue for genomic analysis, clinical researchers advocate a two-tiered system, which would provide tissue for hypothesis-generating studies, while preserving the valuable contents of tissue banks maintained by the cooperative groups.

Working behind closed doors, the Dialogue and NCI are preparing to alleviate the shortage of tissue by the most drastic means imaginable: creating an enterprise that would cost between $500 million and $1.25 billion a year to operate and, presumably, billions to construct. Annual operating costs alone would increase current tissue banking expenditures of the National Institutes of Health by a factor of 10 to 20.

"In size, scope, scientific potential, and the number of potential collaborators, … it is most analogous to the efforts to map the human genome; thus it is more like the space station or a particle accelerator than a traditional medical science initiative," states the unfinished, confidential version of the Dialogue's report proposing the biospecimen network.

If the biospecimen network is created in accordance with plans described in the Dialogue report, it would be exempt from open meetings requirements of the Federal Advisory Committees Act, immune to the provisions of the Freedom of Information Act, and free from federal technology transfer regulations. Meanwhile, the existing, government-funded structures for collecting tissue in the context of clinical trials could be undermined, critics say.

The Dialogue, a non-profit group funded through a combination of public and private funds, entrusted preparation of the project to Paula Kim, a patient advocate who heads the Pancreatic Cancer Action Network, and Jeffrey Trent, president and scientific director of Phoenix-based Translational Genomics Research Institute.

The coordination between NCI and the Dialogue was close:

—Documents show that the Dialogue project involved an "NCI Coordinator," Julie Schneider, an AAAS fellow working in the office of the NCI director.

—In conjunction with the Dialogue effort, NCI awarded a sole-source contract to RAND Corp. to evaluate "selected existing U.S. tissue resources to support and guide the development of a design and engineering plan for a new National Tissue Resource model." Sole-source contracts are unusual at NIH. The RAND study, currently underway, is mentioned repeatedly in the Dialogue's draft report, an indication that the two efforts are coordinated.

—The Institute gave no funding increase to the cooperative groups for fiscal 2003. NCI Director Andrew von Eschenbach announced recently that the groups would undergo a comprehensive, top-to-bottom review, even though a similar review was recently completed. Last week, NCI officials said that some new funds would be found for the group-operated tissue banks for next year, but the magnitude of the increase remains unknown.

—Sources said NCI officials recently revealed a plan to switch the cooperative group-run tissue banks from grant funding to funding through contracts. In principle, this administrative change could allow the Institute to remove control of the tissue banks from the scientific leadership of the cooperative groups, transferring the tissues to contractors, observers said.

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—The boundary between the Dialogue and NCI is muted in part because Institute Director von Eschenbach is one of the founders of the Dialogue and vice chairman of its board of directors. Anna Barker, NCI deputy director for strategic scientific initiatives, also sits on the Dialogue board.

—Last December, six months before the Dialogue's draft proposal was formulated, Anthony Dennis, a member of the group of ad hoc advisors designing the biospecimen network, filed a letter of intent to apply for $8 million in Ohio state funds to set up the network's Midwestern regional hub.

Dennis, who is married to Barker, proposed to serve as the principal investigator of this public-private enterprise. Though no proposal was filed, the letter of intent mentioned a plan to "collect and redistribute tissue."

"Commercial potential is inherent in the formation of the center itself, in the creation of an advanced logistics system to collect and re-distribute tissue and in the creation of the largest human genetics and proteomics database in existence," the letter of intent said. Dennis served on a subcommittee that designed the "business plan and operations" for the network, documents show.

Ohio to cancer pathology is what Fort Knox is to the U.S. gold reserve. The state's academic institutions maintain pathology samples for Children's Oncology Group, the Gynecologic Oncology Group, Cancer and Leukemia Group B, the AIDS Malignancy Consortium, and the Cooperative Human Tissue Network.

In a statement, Dennis said he ultimately dropped out of the application process because "our existing and long-standing tissue resources and clinical centers were sufficiently advanced that we felt that the desired outcomes would emerge without further organization."

Dennis, a microbiologist and entrepreneur, was recently involved in Nutri-Logics Inc., an Internet-based company that sought to sell dietary supplements for cancer prevention. Barker, too, was involved in that venture (**The Cancer Letter**, May 30).

**"Statistical Significance Is Not Our Goal"**

The Dialogue started designing NBN last spring, Kim said.

"We brought together a bunch of people, and we talked about what are the rate-limiting steps to getting drug discovery and development in this country," she said to **The Cancer Letter**. "Tissue seems to be on everybody's menu. That's what I keep hearing from people, and I guess if I didn't keep hearing it over and over, I wouldn't think that there is a need."

In addition to obtaining tissue from cancer patients, the system may follow healthy cohorts, perhaps focusing on high-risk groups and precancerous conditions, Kim said.

The Dialogue-designed system would differ fundamentally from clinical trials, Kim said.

"Statistical significance is not our goal," she said. "If you go to a clinical trial, a biostatistician has to figure out what kind of statistical significance this shows or that shows. What we are talking about here in the NBN is developing a resource [for] the researchers, so they could do their research, a resource that will have tissue, and ultimately, it will be a resource that will have tissue and data."

Only a small percentage of cancer patients enroll in clinical trials. "You have special populations, you have underserved populations, you have areas geographically that are underserved," Kim said, characterizing opportunities for tumor collection. "How many states in the country do we have that do not have comprehensive cancer centers? There is so much opportunity out there. There is a huge percentage of available tissue out there that is going totally untapped."

Kim said the system would track the tissue donors in the following manner:

"In a good situation, you would have a patient who consents to donate a specimen, and they donate the specimen, and along with it is the clinical, annotated data that you need to understand what this specimen represents, and then, along with it, would be the capability to [track] this patient longitudinally, as they undergo their treatment, and that information would ideally be recorded back in, and become further critical annotation to the specimen, so that some time from now somebody is looking at that specimen, they would know the history, they understand the specimen history, and what happened to the patient, and ultimately—if that patient dies—you would know what that patient's cause of death was. You have a whole list of information that you understand about that patient."

According to a document titled "NBN Consumer/User Needs Module Summary as of 6/23/03," acquisition would begin with a two-year pilot project involving three "collection sites" that would start with "ten top adult malignancies, based on

mortality: lung, colorectal, breast, pancreas, lymphoma, ovary, bladder, kidney, stomach, esophagus and hepatic cancers from both primary and metastatic sites."

The network would collect tumor and matched normal tissue in fresh frozen and formalin-fixed preparation, and provide "quality-controlled RNA and DNA, and a baseline DNA array on all or a subset of samples." Also collected would be serum, blood, plasma, and, possibly, urine.

"Response-to-treatment and outcomes data will be linked to specimens," the NBN report states. "RNA amplification and baseline proteomics would not be performed." Also, "laser capture microdissection would be performed on a very limited basis, if at all."

Collecting tumor and following patients outside clinical trials would be a departure from existing standards of evidence-based medicine, experts say.

"Tumor tissue without relevant clinical data is like Niagara Falls without water," said David Johnson, deputy director of the Vanderbilt-Ingram Cancer Center, director of the Vanderbilt Division of Hematology-Oncology, and president-elect of the American Society of Clinical Oncology.

"Simply collecting large quantities of lung cancers—with no knowledge of the patient's status and therapy—may provide some insights like 'X percent of lung cancer patients have PTEN mutations,' but what does that really mean?" Johnson said.

"If we have the relevant clinical data, we might be able to say, 'X percent of lung cancer patients have a PTEN mutation, and these patients respond better to treatment Y, as opposed to treatment Z.' This is the information that patients want to know—and learning this does not compromise the basic science of the project."

While outcomes can be collected and tumors annotated outside clinical trials, the most promising leads are likely to come from rigorously designed experiments, proponents of clinical trials say.

"Translational research is an iterative process swinging 'back and forth' between the laboratory and the bedside," Johnson said. "Good translational research is dependent on both elements being represented in the early planning of a project—including something seemingly as simple as tissue collection.

"A good laboratory experiment and a good clinical trial both require careful thought and preparation. Collecting tumor tissue within the context of a clinical trial marries these two processes and enhances both."

The network plans to collect 250,000 tissue samples in five years, documents show. Estimating that it would cost between $2,000 and $5,000 to collect each specimen, the report states that "even using the low estimate, tracking 250,000 samples is expected to cost $0.5 billion a year."

Using this projection, the high estimate would be $1.25 billion per year, not including the costs of analyzing the samples and the costs of starting this gigantic enterprise. According to the report, NIH spends $53 million a year to maintain its existing tissue banks.

The network would contain both public and private sector components, and would make tissues available at varied prices to pharmaceutical companies and academic researchers, documents show.

"The key question is: Which components will be public, which private, and which mixed?" the report states. "Because this is a government system, there is a rationale for government funding. For the private sector to participate, there must be an opportunity for profit. Public and private funding partners and mechanisms need to be identified; fees will almost certainly be part of the mix."

Kim said NCI would be just one "stakeholder" in the network, which doesn't entitle it to control.

"There is a great deal of benefit to bringing all the sectors together," Kim said. "The patient activists have an important role in this. Academics have an important role. Industry has a role. The government has a role… I see NCI as one partner in this project, just as they should be, and just as other sectors that have come to the table."

The working group has consulted a cross-section of cancer constituencies, Kim said.

"We have invited many, many people, to different meetings, to different teleconferences," she said. "We have had cooperative group participation somewhere along the way. I am very comfortable with the fact that we have given all sectors the opportunities to come to the table and participate in this effort."

The Dialogue committee roster includes 35 people, including five staff members of Constella Health Sciences, a consulting firm. "I am comfortable with the fact that we have gone out to a broad group of people," Kim said. "Where else do you see lay advocates right in the thick of it, of having the

opportunity to participate in the development and the identification of problems and the development of the solutions, and bringing together of all these various sectors? I think it's remarkable."

The proposal should be evaluated based on its content, not the procedure followed in its compilation, Kim said. "The content is really what matters," she said. "Does this report make sense? If it's good information, it's good information."

According to Dialogue documents, the report was to be completed on Sept. 16, but Kim said the group still has a lot of work to do. Documents show that the Dialogue would establish the non-profit entity for the network and seek public and private funding for the venture in 2004. After that, the organizers of the network would proceed to development of Requests for Proposals.

Since $500 million to $1.25 billion a year is a significant sum, some NCI programs will surely be cut, and chairmen of the Institute's cooperative groups say they fear for the future of their programs. Group chairmen warn that NCI is embarking on construction of a costly, speculative system for generating hypotheses while jeopardizing the existing, functional system for verification of hypotheses.

"I don't think anyone is looking at tearing anything apart, quite frankly," Kim disagrees. "I think what we are trying to do is build a resource that we feel there is a tremendous need for."

**Report Urges Study of Existing Resources**

The authors of the Dialogue report argue that existing tissue banks are woefully inadequate.

"Although existing resources are plentiful (there are approximately 350 organizations with more than 300 million tissue samples representing almost 160 million cases), materials are in various states of usefulness and readiness, no standards exist across the board, patient consent varies, fresh tissue is not readily available, and annotation of fresh tissue is rare," the report states. "The extent to which parallel systems can or should be maintained and how the value of all resources can be maximized require further study. It was agreed that an enormous amount of money is currently being paid for tissue resources, and it will be difficult to stop the flow of these funds."

The cooperative groups have been collecting tumor tissue for over three decades, and, naturally, tissues obtained in the 1970s would be more challenging to work with than tissues obtained last year. However, even 30-year-old specimens can be analyzed through rapidly-evolving genomic techniques to provide information that is likely to help develop cancer therapeutics.

In recent years, samples have been collected based on standards that are close to uniform, group chairmen say. Obtaining the samples, controlling treatments, tracking the outcomes, and assuring informed consent is part of the day-to-day functions of the cooperative groups.

"If the goal is to develop something like a space station, we must remember that billions have been invested so far in the space station, and we still don't have one that is functional," said Richard Schilsky, chairman of Cancer and Leukemia Group B and chairman of the NCI Cooperative Group Chairs Committee.

Schilsky agrees that researchers need better access to tumor tissues. To solve this problem, he suggests a simple two-tiered system.

"The highest level specimens are those obtained by the groups, because of the clinical annotation that comes with those samples," Schilsky said. "Because the group specimens are so valuable, we also need a second tier of tissue collection that provides tissue and much more limited clinical data such as patient demographics, diagnosis, and survival. These tissues, currently collected by Cooperative Human Tissue Network, would allow for hypothesis-generating experiments, the results of which would fuel the next generation of definitive trials by the groups."

The group-run tissue banks are not uniformly organized, but they have adopted a set of standards. This was accomplished through the work of the Intergroup Specimen Banking Committee.

"All the groups are now making tissue microarrays from paraffin blocks rather than cutting sections from individual blocks," Schilsky said. "As the technology continues to improve, it will become less important to collect frozen tissues, as most all macromolecules will be recoverable from paraffin."

The cooperative groups need additional resources, Schilsky said. "Many of the groups have limited frozen tissue banks," he said. "For example, in CALGB, we have leukemia specimens and lung cancer specimens. What has held the groups back has been lack of sufficient funding to bring their banks and collection systems to the next level."

Allowing the groups to fulfill their potential would be considerably less expensive than Dialogue's system, said Schilsky, who was asked by **The Cancer Letter** to review the NBN proposal.

"We already have the infrastructure to accomplish the major goals of NCI if we just fund it adequately," he said. "If the NBN diverts funds from the groups, it will do much more harm than good."

Assuring uniformity of standards for preserving tissue is a small part of the enterprise of running a tissue bank, said an executive at a biotechnology company involved in genomics research. The executive spoke on condition of anonymity, after reviewing the Dialogue proposal, which was provided by **The Cancer Letter**.

"Preservation is a straightforward mechanical process," the executive said. "A high-quality repository should be able to obtain and maintain its specimens for $200 per case. The real expense here is the manpower and the informatics commitment needed for rigorous follow-up.

"My biggest question in all of this is the nature of this half-billion-dollar amount. Why are they reinventing the wheel from scratch, instead of improving on existing structures?"

**"Legacy Systems"**

"The Working Group members agreed that an NBN could not take responsibility for what has been collected by others," the Dialogue report states. "The achievement of standardized results with a rigorous molecular profile requires tissue collection under highly standardized procedures. A majority of the Working Group believed that inclusion of legacy systems in the national model would be difficult… This is not to say that legacy resources are not of value; a catalog of these other valuable resources should be part of the NBN system. They may well be suited for specific needs. However, the NBN focus should be prospective."

The report notes that the NCI-funded RAND study would help determine the fate of existing tissue banks.

"It is suggested that a legacy system committee consist of representatives from all categories: users, tissue resource workers, government, scientists, patient advocates, and consultants," the report states. "Additionally, material from the 2003 RAND study may inform the decisions that will be necessary."

In April, NCI announced the impending award of the contract to RAND. The text of the announcement follows:

"The National Cancer Institute, Office of Science Planning and Assessment plans to enter into a sole source contract with RAND Corp.… The purpose of this project is to provide a written evaluation of selected existing U.S. tissue resources to support and guide the development of a design and engineering plan for a new National Tissue Resource model.

"This effort is a collaborative project and jointly funded by the National Cancer Institute and the National Dialogue on Cancer. The evaluation will consider a collection of government, academic, and private sector tissue repositories to identify `best practices,' and assess whether these resources could be adapted to fulfill the requirements of a new model for a National Tissue Resource.

"In 1999, RAND Corp. published a supplement to a National Bioethics Advisory Commission Report about the ethical and policy issues relation to research on human biological materials. Dr. Elisa Eiseman, an employee of RAND, was the Principal Investigator of the study and this proposed evaluation of selected existing U.S. tissue resources builds upon that effort and relies heavily on the previously-collected data.

"This is not a request for competitive proposals."

RAND employees have been contacting cooperative groups and pathology companies in recent weeks, sources said.

**The Ohio Plan**

According to the Dialogue report, a non-profit group would run the national system and handle the informatics at a central office. Satellite offices around the U.S. would store the tissue.

Preparations for administering this system appear to have begun long before the Dialogue completed its draft report. The Dialogue report was dated May 28, 2003.

Six months earlier, on Dec. 13, 2002, ad hoc group member Dennis submitted a letter of intent to seek $8 million in Ohio state funds for creation of a "National Oncology Tissue Repository and Genetic/ Proteomic Database."

Dennis is president of Omeris Inc., a Columbus-based non-profit organization funded partly by the Ohio Department of Development. Earlier that month—on Dec. 4, 2002—Von Eschebach announced that Dennis's wife Barker was appointed NCI deputy director for strategic scientific initiatives. For months prior to taking that job, Barker served as a consultant to von Eschenbach (**The Cancer Letter**, Dec. 6, 2002).

The letter of intent described Dennis as the principal investigator of the proposed venture that

would include NCI, the Dialogue, and the International Genomics Consortium, an Arizona-based entity founded by Trent, co-chairman of the Dialogue working group. Other applicants listed included The Ohio State University, James Cancer Center, The Ohio Hospital Association, Children's Hospital of Columbus, Battelle, BioEnterprise, Rescentris, Acero, Proctor & Gamble Pharmaceuticals, Roche, and Eli Lilly.

Investigators at Columbus Children's Hospital apparently didn't consent to participate in the Ohio tumor registry project, said Gregory Reaman, chairman of the Children's Oncology Group, who looked into the matter after being contacted by a reporter.

Last fall, investigators at Children's declined Dennis's invitation to collaborate, in part because his proposal required them to provide a staff member for the endeavor, Reaman said. Staff members at the tissue bank are paid under NCI grants, and cannot be shifted to other tasks.

The investigators were assured that the project would be abandoned, and were apparently unaware of the letter of intent, Reaman said. The hospital also stores tumors for the Gynecologic Oncology Group. The letter of intent mentions "re-distributing" tissues.

"Why would we want another initiative to railroad what we think is already a good—albeit underfunded—system?" Reaman said. "We have a system of tissue procurement and banking that is integrally linked to a very robust clinical database, for which in every single pediatric cancer disease category there are active translational research activities."

Though no application was filed, the text of Dennis's letter of intent, a public document, is indicative of the state of knowledge about the biospecimen network six months prior to completion of the Dialogue draft. The text of the document follows:

"The Repository would be the Midwest regional (multi-state) center for acquiring, genetically analyzing, utilizing and distributing normal and tumor tissues from 50,000+ cancer patients to researchers in academic and private organizations in the U.S.

"The purpose of the tissue repository is to significantly accelerate the discovery and development of therapies and prevention strategies for cancer by providing a large, easily accessible repository of uniformly collected, clinically annotated, genetically and proteomically characterized tissues and their associated data.

"The bulk of the cancer data would be provided on a pre-competitive basis (accessible to all potential users in the private, public and academic sectors). The highly characterized data related to other disease states such as heart disease, diabetes, obesity, etc. inherent in such a large human disease database will be used as the basis for proprietary technology development, drug target development, new company formation or licensing to large pharmaceutical firms.

"The center would be one of a small handful of (or the sole) national tissue repositories in the U.S. established cooperatively by federal, state and private funds. The repository would operate an advanced collection, distribution and analysis center and through agreements with state and regional hospitals would place data collection capabilities at all locations advancing the connectivity among regional medical centers.

"The center will leverage significant federal and private funds. The center will represent a new state of the art in bioinformatics with complete genetic profiles of thousands of human patients coupled to annotated clinical data and made available on-line in a useful format for researchers nationwide.

"Advanced logistics for the management of tissue acquisition and re-distribution will be developed. The full database of information will hold statistically valid genetic and proteomic data on most common adult diseases, which can be of great value for both new commercial ventures and for established pharmaceutical companies.

"The potential to nurture genomics, proteomics, bioinformatics and other developing capabilities in Ohio's start-up and established companies is enormous as is the potential for significantly reducing the social and economic impact of cancer. This concept emerged as a high priority element of a national dialog on cancer, which gathered more than 100 of the leading government, academic and industry representatives in Washington, D.C., early in 2002.

"Ohio is extremely well suited to pursue this national center either alone or in conjunction with a developing center in Arizona.

"Commercial potential is inherent in the formation of the center itself, in the creation of an advanced logistics system to collect and re-distribute tissue and in the creation of the largest human genetics and proteomics database in existence.

"The existence of the center will attract the interest of major pharmaceutical and biotechnology

companies and will create licensing and company creation opportunities in numerous disease areas for both therapy and prevention. The formation of the center will have the secondary benefit of creating an extensive collaboration among numerous Ohio organizations and creating a state-of-the-art digital data acquisition system among a broad array of regional hospitals."

Dennis declined a request for an interview and responded to a reporter's questions with a written statement.

"I was pleased to serve as an early volunteer on the working group that identified this concept at an NDC research meeting on removing barriers to genomics/proteomics based research," Dennis wrote.

"Although this is an exciting and timely idea, it is not a new concept, as other countries, private organizations, and academic institutions are pursuing similar strategies around the globe. As to my role, a couple of individuals were invited to attend the original exploratory sessions to represent states with significant clinical and supportive core resources.

"Ohio has such significant capabilities in these areas and in clinical medicine. In fact, Ohio leads the nation in many clinical science categories and has so for many years. I was able to participate in a very limited way due to demands on my time, but no longer have the time to participate, and recently resigned as a member of the planning group.

"Given Ohio's significant breadth and depth of resources in existing tissue repositories, and the fact that Ohio is the No. 1 state in the nation for per capita clinical trials of all types, we have considered several options for deploying our resources to support the advancement of healthcare and the bioscience industry in our state," Dennis wrote.

"You asked about a non-binding letter of intent that we submitted to the state as part of our planning process for potentially uniting our distributed clinical trails capability—with our nationally recognized tissue repositories as part of those resources. The submission of such 'placeholders' is common practice, and the state receives a number of these in any round of submissions. After completing our planning late last year, we elected not to follow up on this letter of intent with a formal proposal, as our existing and long-standing tissue resources and clinical centers were sufficiently advanced that we felt that the desired outcomes would emerge without further organization.

"However, I believe that if you speak with individuals who have volunteered to work on the concept of a national biospecimen network to support 21st century science, everyone did so unselfishly to create something of real value for the scientific community and for cancer patients," Dennis wrote. "It is an extraordinary group of individuals with in-depth knowledge and capability from all sectors interested in the issue."

Kim said she was unaware of Dennis's letter of intent. "I know that there are several states around the country that have been really terrific at taking a hard look at the tissue issues in their respective states, to see what can be done on the statewide level to facilitate researcher needs in a way of tissue specimens," she said.



## The Cancer Letter Takes Summer Publication Break

**The Cancer Letter** takes its annual summer publication break for the next four weeks.

The next issue of **The Cancer Letter** is scheduled for publication on Sept. 12.

**Business & Regulatory Report** is not published in August. The next issue is scheduled for publication in September.

THE CANCER LETTER

Vol. 18 No. 7
July 2003

# Business & Regulatory Report

*Deals & Collaborations:*

## Corixa, MDS Sign Manufacturing Agreement For Radiolabel of Antibody In Bexxar

**Corixa Corp**.(Nasdaq: CRXA) of Seattle and **MDS Nordion** (NYSE: MDZ; TSX: MDS) of Ottawa, Ontario, said the companies have signed a new seven-year manufacturing agreement in which MDS Nordion will continue to radiolabel the antibody in Bexxar (tositumomab and iodine I-131 tositumomab) therapy.

Bexxar therapy is an investigational radioimmunotherapy being co-developed by Corixa and GlaxoSmithKline and is in the final stages of

(Continued to page 2)

*Clinical Trials:*

## Aton Begins Testing SAHA For Leukemia; AstraZeneca Opens Phase III EFECT Study

**Aton Pharma Inc**. of Tarrytown, NY, said enrollment has begun in a phase I trial of SAHA for advanced leukemias, including acute myeloid leukemia, chronic myeloid leukemia, acute lymphocytic leukemia, and chronic lymphocytic leukemia, as well as myelodysplastic syndrome.

SAHA is an inhibitor of histone deacetylase, the company said.

The open-label study, which will be conducted at The University of Texas M. D. Anderson Cancer Center, would establish a safety profile and dosing schedule in 20 to 30 adult patients, the company said. A secondary objective is to evaluate the anti-tumor activity. In addition, the study will examine the biological effects of SAHA in peripheral mononuclear cells and bone marrow blast cells, the company said.

The agent is being studied in two phase II trials, one for cutaneous T cell lymphoma or peripheral T-cell lymphoma and another for recurrent or metastatic squamous cell cancer of the head and neck, the company said.

* * *

**AstraZeneca** (NYSE: AZN) of Wilmington, Del., said it has begun recruitment in a randomized, double-blinded phase III trial on the efficacy and tolerability of Faslodex (fulvestrant) Injection vs. exemestane in postmenopausal women with hormone receptor-positive metastatic breast cancer whose disease has recurred or progressed on treatment with a nonsteroidal aromatase inhibitor.

The EFECT trial (Evaluation of Faslodex vs. Exemestane Clinical Trial) will enroll 660 women from100 to 150 centers in the U.S. and elsewhere, the company said. Participants will be randomly assigned to

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Reminder to Subscribers:
Business & Regulatory Report is not published in August. The next issue will be published in September.

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## Genedata, Singapore Center, Enter Research Collaboration

(Continued from page 1)

regulatory review by FDA, the companies said.

The therapy contains a radiolabeled antibody (tositumomab), that is linked to an isotope (I-131), the companies said.

Under a separate agreement, Boehringer Ingelheim Pharma KG produces bulk tositumomab, which is sent to MDS Nordion for radiolabeling, the companies said.

The supply agreement replaces the existing development, supply and facilities agreements entered into in 1995 and 1998, respectively, the companies said.

* * *

**Genedata** of Basel, Switzerland and the **National Cancer Centre** of Singapore said they have entered into collaboration in gene expression analysis for cancer research.

As part of the agreement, NCCS has licensed the expressionist system for the analysis of microarrays, the companies said.

NCCS will identify minimal sets of diagnostic marker genes for classifying tissues and different cancer types into subclasses, the companies said. The system would also identify the function of genes in tumor development and progression, understand the biological processes for tumor progression, and characterize oncogenic signal transduction pathways.

"It will only be possible to develop commercially viable diagnostic tests that physicians can routinely use if we can minimize the complexity of such diagnostic tests by focusing on the most relevant marker genes," said Patrick Tan, principal scientist at the Division of Cellular and Molecular Research. "Genedata offers a comprehensive system that addresses the most critical issues in diagnostics based on gene expression profiling, namely quality control, data standardization, and sophisticated biostatistical analysis."

Genedata specializes in scientifically validated software systems and computational solutions for the drug discovery industry.

* * *

**Genzyme Corp.** (Nasdaq: GENZ) of Cambridge, Mass., and **SangStat Medical Corp.** (Nasdaq: SANG) of Fremont, Calif., said they have reached an agreement under which Genzyme will acquire SangStat in an all cash transaction valued at $22.50 per outstanding share, or approximately $600 million.

Genzyme said it is acquiring a company with antibody product used in organ transplantation and a pipeline in immune suppression and immunology. The pipeline is complementary to its own work in immune-mediated diseases, such as scleroderma, multiple sclerosis, and pulmonary fibrosis.

The SangStat lead product, Thymoglobulin (anti-thymocyte globulin), is indicated in the U.S. for acute rejection of a renal transplant, the companies said.

The company reported revenues of $120 million in 2002, generating earnings of $0.24 per share.

Thymoglobulin is an immunosuppressive polyclonal antibody product for acute organ rejection in transplant patients, the companies said. Clinical studies have demonstrated Thymoglobulin may reverse an acute rejection episode.

The acquisition is in the form of an all cash tender offer, which could be in effect by early September, the companies said.

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**Geron Corp.** (Nasdaq: GERN) of Menlo Park, Calif., said it has completed its genomics research collaboration with **Celera Genomics Group** (NYSE: CRA) of active genes in human embryonic stem cells.

The research has yielded physical libraries of cloned mRNA transcripts that are expressed in undifferentiated hESCs and in partially differentiated cell populations derived from hESCs, the company

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said. DNA sequence analysis led to a database, which can identify and assign function to genes in early human development, and that support development of small molecule pharmaceuticals, protein therapeutics, cell and gene therapies, diagnostics, and tools in drug discovery and testing.

The collaboration combined the Geron hESC biology with the Celera DNA sequencing and gene discovery capabilities, the company said. Libraries of cDNA clones were produced from undifferentiated hESCs and three partially differentiated cell populations derived from hESCs. From the gene libraries, over 148,000 individual cDNA clones were sequenced representing more than 32,000 genes in the human genome. The sequence information resulted in a searchable, database of gene expression information that can identify genes preferentially associated with the undifferentiated state of hESCs and demonstrates changes in the activities of individual genes during the early stages of differentiation, the company said.

hESCs are immortal, undifferentiated cells that form all other cells and tissues in the body, the company said. Geron funded the research by James Thomson at the University of Wisconsin-Madison that resulted in the first isolation of hESCs.

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**IDM** of Paris said it has exercised its option, under an evaluation and license option agreement, to a non-exclusive license from **Epimmune Inc.** for cancer epitopes in its ex vivo cell therapy program.

Under the original agreement of October 2002, IDM had the right to evaluate the epitopes and exercise its option to license patented and non-patented rights to the Epimmune universal cancer epitope packages to use with the IDM ex vivo dendritic cells technology, the company said.

IDM said it elected to exercise its option based on the results of its preclinical studies, which evaluated the stimulation of specific cytotoxic T cells using peptide loaded dendritic cells. The territory is worldwide except for Japan where IDM maintains an additional option to exercise a license.

IDM has filed an IND application with FDA for a phase I/II trial on its cell drug Collidem using a selection of Epimmune epitopes for colorectal cancer, the company said. If approved, the trial would take place in the U.S., under the management of IDM Inc., a subsidiary of IDM of Irvine, Calif.

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**ImClone Systems Inc.** (NASDAQ: IMCL) of New York said it has achieved two equity-based milestones totaling $6 million in its Erbitux license agreement with **Merck KgaA**.

The milestones were triggered by the Merck KGaA submission of applications for authorization to market Erbitux for metastatic colorectal cancer in the European Union and Switzerland, the company said. The Merck KGaA regulatory submissions were made with the European Agency for Evaluation of Medicinal Products, the pharmaceutical regulatory body of the E.U., and with Swissmedic, the Swiss agency for therapeutic products.

ImClone will receive a milestone payment of $3 million for each of the two submissions, whereupon, the company will issue 92,276 shares and 90,944 shares of its common stock to Merck KGaA for the Swiss and European Union submissions respectively, the company said. Both issuances will represent the sale at a ten percent premium to market value at the time each milestone was achieved, as provided in the companies' license agreement.

In December 1998, Merck KGaA licensed from ImClone Systems the right to develop Erbitux outside of the U.S. and Canada and the co-exclusive right to develop the drug in Japan, the company said.

"We look forward to a continued collaboration with both Merck KGaA and Bristol-Myers Squibb, and to submitting a biologics license application to FDA in the second half of 2003 for U.S. approval of the drug for metastatic colorectal cancer," said Daniel Lynch, acting CEO of ImClone Systems Inc.

Erbitux (cetuximab) is an investigational IgG1 monoclonal antibody that targets and blocks the epidermal growth factor receptor, which is expressed on the surface of cancer cells in multiple tumor types, the company said.

**In an update,** Imclone said it has now received a $3 million payment from Merck KGaA for achieving a clinical development milestone under the license agreement for Erbitux. Upon payment, ImClone Systems said it issued 150,007 shares of its common stock to Merck KGaA, representing the sale of the shares at a ten percent premium to market value as provided in the license agreement.

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**Kosan Biosciences Inc**. (NASDAQ: KOSN) of Hayward, Calif., said it has initiated phase Ib clinical trials of 17-allylamino-geldanamycin (17-AAG) in combination with other anti-cancer agents under a cooperative research and development agreement with the NCI Cancer Therapy Evaluation

Program.

The trials initiated to date include 17-AAG in combination with gemcitabine and cisplatin for solid tumors, with imatinib mesylate (Gleevec) for chronic myeloid leukemia, and with docetaxel (Taxotere) for advanced solid tumors, the company said.

Under the CRADA, additional phase Ib combination trials and phase II monotherapy trials of 17-AAG would begin by the end of 2003, the company said.

17-AAG inhibits Hsp90 (heat shock protein 90), a protein chaperone that binds to several sets of signaling proteins, known as client proteins, the company said. The proteins include targets such as mutated p53, Bcr-Abl, Raf-1, ErbB2 and others. When 17-AAG binds to Hsp90 it causes disruption of the Hsp90-client protein complexes, which in turn leads to their degradation by the proteosome.

Preclinical studies suggest that the drug sensitizes cancer cells to other anti-cancer agents, the company said.

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**Oncolytics Biotech Inc.** (TSX: ONC, NASDAQ: ONCY) of Calgary said it has entered into a research collaboration with Ramon Alemany of the **Institut Catala d'Oncologia**, of Barcelona, Spain, to develop modified adenoviruses that are selective for Ras mediated cancers.

"Two-thirds of human cancers have some form of mutation that leads to Ras activation, adding a new generation of viruses that are designed to be selective for RasAS mediated tumours will expand our oncology focus." Said Matt Coffey, vice president, product development of Oncolytics. "Alemany has been influential in the development of additional viral constructs for clinical development."

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**Panscopic** of San Francisco said **Tularik** of South San Francisco has chosen the Panscopic application, a self-service reporting solution, to automate its research processes.

The application allows accelerated research processes by means of flexible, self-service reporting and analytics, the company said.

Tularik develops orally available medicines that act through the regulation of gene expression, the company said. The solution would enable researchers to analyze and interpret laboratory test data, without relying on IT development resources.

"The Panscopic application best fits the nature of our J2EE environment and makes it easy to work with XML and Oracle data," said Bruce Ling, director of research informatics at Tularik.

The application enables readers to analyze and interpret data over the Web, the company said. Reports are parameterized and flexible, so that data can be manipulated on the fly to fit the needs of the reader and project. Easy-to-use charting and graphing capabilities have also eliminated the need for readers to pull data into Microsoft Excel. Eliminating this step has also helped to reduce errors and misinterpretations of the data, the company said.

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**Quest Diagnostics Inc.** (NYSE: DGX) of Teterboro, N.J., said it would sponsor the distribution of the **National Comprehensive Cancer Network** CD-ROM on cancer testing guidelines for non-cancer specialists.

The guidelines cover cancer-related testing for more than 100 different cancers and focus on work-up and follow-up testing, and ongoing monitoring following therapy, the company said. Additional goals are to facilitate primary care physicians' understanding of the rationale for a specific set of tests.

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**SciTegic Inc.** of San Diego said that **Chiron Corp.** has purchased a multi-user license to Pipeline Pilot, a software application that allows compound library acquisition and activity modeling for optimizing high-throughput screening.

Chiron has purchased the Pipeline Pilot technology for multiple internal users, as well as a license for the SciTegic Web interface that allows a greater number of additional users using a Web browser.

Pipeline Pilot is a technology that integrates and automates drug discovery informatics data processing, the company said.

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**Siemens Medical Solutions** of Siemens AG (NYSE: SI) of Malvern, Pa., said it has made an equity investment in **VisEn Medical Inc**. of Woburn, Mass., to develop applications of molecular imaging to accelerate drug development and improve early disease detection and characterization.

Molecular imaging allows non-invasive measurement of molecular and biological processes within the body, the company said. Compared to conventional diagnostic imaging, molecular imaging probes the molecular abnormalities that are the origin of disease, rather than imaging the resulting conditions

or morphologies caused by the disease.

"The long term goals are the development of both systems and agents to expand the markets for in vivo imaging of molecular events in the research and clinical marketplaces," said Guy Mayer, CEO of VisEn.

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**SRI International** of Menlo Park, Calif., said it has been awarded a two-and-a-half-year exploratory/developmental R33 Fast-Track grant by NCI to develop in vitro assays using hepatobiliary cell systems.

The assays would identify toxicological profiles and predict safety of therapeutics for cancer and other diseases, the company said.

SRI said it is building assays around multicellular systems with good survival in culture and the capability to model liver injury and response. The modified technique extends liver cell viability to 10 days or more, instead of two to three days, in combination with classical biomarkers to predict the relative toxicity and target cell specificity of liver toxicants. The advance allows researchers to perform longer-term cell incubations in studying chronic liver exposures and effects such as fibrosis, the company said.

Alison Vickers, of the Novartis Institute for Biomedical Research, identified the techniques for improved slice preparation and culture conditions, the company said.

"Our approach can lead to better-informed predictions on the nature and severity of liver damage in humans," said Charles Tyson., director of the SRI Advanced In Vitro Toxicology program and the principle investigator. "Performing the assays in vitro facilitates extrapolation of adverse effects in animals to humans before clinical testing, for better confidence in lead drug selection,"

The grant stems from work performed by SRI under an R21 grant that began in 2002, the company said. SRI received the follow-on R33 grant after it demonstrated the feasibility of its approach. The total amount of the SRI R21/R33 phased award is $1.82 million, which represents 100 percent of the total costs for the project.

*Product Approvals & Applications:*

## EU Grants Orphan Drug Status To Aphton Corp.'s G17DT

**Aphton Corp.** (Nasdaq: APHT) of Miami said the European Union has granted orphan drug status to its anti-gastrin immunogen G17DT, also known as G17(9)DT, for both pancreatic cancer and gastric cancers.

FDA granted orphan drug status to its immunogen G17DT in July 2002 for both pancreatic cancer and gastric cancer indications, the company said.

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**Axcan Pharma Inc.** (Nasdaq: AXCAS) of Mont Saint-Hilaire, Quebec, said it has received approval from U.S. FDA to use Photofrin photodynamic therapy in the ablation of High-Grade Dysplasia in Barrett's Esophagus where esophagectomy has not been performed.

Photofrin PDT was also granted orphan drug designation for the indication, which guarantees a 7-year marketing exclusivity, the company said.

"We expect to launch Photofrin PDT in the U.S. at the beginning of fiscal 2004 and to reach peak sales of U.S. $30-50 million within 5 to 7 year," said Leon Gosselin, president and CEO of Axcan.

Photofrin PDT was approved in Canada for the ablation of HGD in Barrett's Esophagus and is still under review in Europe for a similar indication, the company said. Axcan said it is supporting phase II studies of Photofrin PDT for cholangiocarcinoma, cancer that grows in the ducts that carry bile from the liver to the small intestine.

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**Cephalon Inc** said FDA has approved a compressed powder formulation of Actiq (oral transmucosal fentanyl citrate) [C-II]for breakthrough cancer pain for those with malignancies already receiving and are tolerant to opioid therapy.

The formulation is bioequivalent to the previous formulation, with dosage strengths printed on the handle tag, the company said.

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**Eli Lilly and Co.** of Indianapolis said regulatory officials in Finland approved an expanded indication for Gemzar (gemcitabine HCl) in combination with Taxol (paclitaxel) for unresectable, locally recurrent or metastatic breast cancer that has relapsed following adjuvant or neoadjuvant chemotherapy.

Based on a submission in December, the indication requires prior chemotherapy and should have included an anthracycline unless clinically contraindicated, the company said.

"Gemzar has proven its efficacy in clinical trials that support multiple indications in solid tumor

treatment. The combination offers women an increased amount of time until the disease spreads or worsens," said Paolo Paoletti, vice president of oncology products, Eli Lilly and Co.

Approval is based on interim analysis of data gathered from an ongoing phase III trial of the Gemzar/Taxol combination compared to single-agent Taxol for metastatic breast cancer. A U.S. regulatory submission for Gemzar for metastatic breast cancer is being discussed, the company said.

The primary endpoint of the trial is overall survival, the company said.

The global study of 529 women previously treated with an anthracycline with no prior chemotherapy in the metastatic setting yielded the following results: Gemzar/Taxol combination delayed progression of the disease compared to single-agent Taxol (5.4 months vs. 3.5 months, p= 0.0013). Oververall response rate, was also better with the Gemzar/Taxol combination (39.3 percent vs. 25.6 percent, p= 0.0007). Non-hematologic toxicity was moderate in both arms. Grade IV hematologic toxicity was more pronounced in the combination arm, with the most common side effect being a decrease in white blood cells (17.2 percent vs. 6.6 percent, p= 0.0002), the company said.

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**Genentech Inc.** (NYSE: DNA) of South San Francisco said it has received Fast-Track designation for Avastin (Bevacizumab, rhuMAb-VEGF) for previously-untreated first-line metastatic colorectal cancer.

Avastin is an investigational therapeutic antibody that inhibits vascular endothelial growth factor, a protein that induces tumor angiogenesis, the company said. By inhibiting VEGF, the antibody interferes with the blood supply to tumors.

"The Fast Track designation will allow for a rolling submission of our biologics license application, which allows for ongoing submission of materials that can facilitate the review process," said Susan Hellmann, executive vice president, development and product operations, and chief medical officer at Genentech.

The designation is based on results from a phase III multicenter, randomized and blinded study, the company said. The trial enrolled more than 900 patients, and randomized 800 patients to receive either Avastin plus the standard of care chemotherapy (5-FU/Leucovorin/CPT-11, called IFL) or the IFL regimen plus an Avastin placebo. A third arm of the study treated 110 patients with Avastin plus 5-FU/ Leucovorin chemotherapy. That arm was dropped, as pre-specified, once adequate safety with the IFL regimen was established, the company said.

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**Helsinn Healthcare SA**, of Lugano, Switzerland, said FDA has granted marketing approval for palonosetron for the prevention of acute nausea and vomiting associated with initial and repeat courses of moderately and highly emetogenic cancer chemotherapy, and the prevention of delayed nausea and vomiting associated with initial and repeat courses of moderately emetogenic cancer chemotherapy.

"The new indications for palonosetron advance the standards of therapy for delayed emesis due to moderately emetogenic chemotherapy," said Steven Grunberg, lead consultant on the palonosetron pivotal program and professor of medicine and pharmacology, Fletcher Allen Healthcare, University of Vermont. "Palonosetron is the first 5-HT3 receptor antagonist to be granted approval for prevention of delayed emesis with a single dose in this patient population."

The drug will be commercialized under its new trademark Aloxi in U.S. by the Helsinn licensee MGI Pharma, the company said.

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**Merck KGaA** (FWB:MRK) of Darmstadt, Germany, said it has filed marketing authorization applications with the European Agency for the Evaluation of Medicinal Products with Swissmedic for Erbitux (cetuximab) for metastatic colorectal cancer.

Merck is seeking approval of cetuximab as a monotherapy and in combination with the standard chemotherapy irinotecan, the company said. Upon approval for an accelerated registration procedure, marketing authorization across the European Union could occur in 2004.

The MAAs include the results of the BOND study, the company said. Merck said it licensed the right to market cetuximab outside of the U.S. and Canada and the co-exclusive right to market cetuximab in Japan from ImClone Systems Inc. in 1998.

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**OXiGENE Inc.** (NASDAQ: OXGN, XSSE: OXGN) of Watertown, Mass, said FDA has awarded orphan drug status to Combretastatin A4 Prodrug for anaplastic thyroid cancer and for medullary, stage IV papillary and stage IV follicular thyroid cancers.

CA4P is in a phase II trial for advanced ATC, one of four concurrent oncology studies of the drug candidate, the company said.

"As we advance CA4P to market, the orphan drug designation—and FDA Fast Track designation we announced last month—represent key building blocks in our clinical development and commercialization strategy," said Fred Driscoll, president and CEO of OXiGENE.

In phase I safety trials of CA4P, completed in 2001, one patient with ATC responded completely to CA4P as a single-agent treatment, the company said. The patient has been disease free for more than 44 months. One phase I patient with medullary thyroid cancer experienced 17 months of disease stabilization, while a second medullary patient remained stable for one year.

"Thyroid tumors are known to be highly vascularized, and thus we believe they may be particularly susceptible to the blood-flow blocking effects triggered by vascular targeting compounds such as CA4P," said Scott Young, vice president of clinical and regulatory affairs at OXiGENE. "The orphan drug designation that includes multiple forms of thyroid cancer provides us with incentive to evaluate the clinical development of CA4P in these other thyroid tumor types."

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**Seattle Genetics Inc.** (Nasdaq:SGEN) of Bothell, Wash., said FDA has granted orphan drug designation to its product candidate SGN-30, a monoclonal antibody, for Hodgkin's disease.

SGN-30 is in an ongoing phase I/II trial for CD30-positive hematologic malignancies, including Hodgkin's disease, anaplastic large cell lymphoma and other types of lymphomas.

"The drug designation strengthens our SGN-30 program by offering several important clinical development and commercialization benefits," said Clay Siegall, president and CEO of Seattle Genetics.

**In another delevelopment,** Seattle Genetics Inc. and **Genencor International Inc.** (Nasdaq: GCOR) of Palo Alto, Calif., said they have agreed to extend and modify terms of their collaboration agreement established in January 2002.

Under the amended agreement, Genencor will pay Seattle Genetics a fee to extend the term of the collaboration by two years and obtain a non-exclusive license to the Seattle Genetics proprietary antibody-directed enzyme prodrug therapy technology for multiple targets, the companies said. Genencor has also agreed to co-fund a portion of the SG prodrug program. SG continues to have rights of access to the Genencor i-mune technology for any ADEPT molecules it is developing. Each party can independently develop products utilizing the other party's technology, subject to payment of fees, milestones and royalties on net sales of independent products. Seattle Genetics will continue research and development of its lead ADEPT product candidate, SGN-17/19, on its own without further co-funding from Genencor, the companies said.

"With our ADEPT technology we are developing classes of prodrugs designed to be stable in the bloodstream yet potent against tumor cells," said Clay Siegall, president and CEO of Seattle Genetics.

ADEPT treats cancer through two-step combination of two non-toxic agents to achieve antitumor activity, the companies said. In the first step, monoclonal antibody fragments genetically fused to enzymes are administered and accumulate within tumor tissues. In the second step, a relatively inactive form of an anti-cancer drug (a prodrug) is administered and is converted by the enzymes into a cancer cell-killing drug.

## *Patents:*

## Adherex Issued Patent For Anticancer Compounds

**Adherex Technologies Inc.** (TSX:AHX - News) of Ottawa said it was issued a U.S. patent for compounds that inhibit cancer metastasis via OB-cadherin (cadherin-11) antagonism.

"The abnormal presence of OB-cadherin in tumor cells has been found to be linked to cancer metastasizing to distant sites," said Orest Blaschuk, chief scientist and co-founder of Adherex. "The compounds covered by this patent are able to bind OB-cadherin in tumor cells and could prevent the spread of cancers."

Laboratory studies at the Georgetown University Lombardi Cancer Centre have shown that Adherex OB-cadherin antagonists block cancer cell migration.

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**Lorus Therapeutics Inc.** of Toronto said the Canadian Patent Office has approved patent protecting its intellectual property for discovery and use of antitumor oligonucleotide molecules that target the stability of messenger RNA (mRNA) molecules that code for proteins involved in essential cellular functions.

*Clinical Trials:*

## Faslodex Vs. Exemestane For Recurrent Breast Cancer

(Continued from page 1)

receive 250 mg injection of the treatment administered every 28 days (an initial 500 mg injection on day zero followed by 250 mg injection on days 14 and 28, and once monthly thereafter) or 25 mg of exemestane (a steroidal aromatase inhibitor) administered once daily as a tablet, the company said.

"Previous trials in this patient population have been in post-tamoxifen failures," said William Gradishar, EFECT international coordinating investigator, and associate professor of medicine and director of breast medical oncology, Robert H. Lurie Comprehensive Cancer Center, Northwestern University. "EFECT is an important trial that will help us understand the sequencing options for hormone receptor-positive metastatic breast cancer."

Faslodex is approved in the U.S. for hormone receptor-positive metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy such as tamoxifen.

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**BTG** of Philadelphia said it plans to develop BGC 9331 for gastric and pancreatic cancers.

The drug, formerly known as ZD9331, was a collaboration between the Cancer Research UK Centre for Cancer Therapeutics at The Institute of Cancer Research, Sutton, UK, AstraZeneca UK Ltd and BTG, the company said.

AstraZeneca was granted rights to develop and market the drug and undertook a pre-clinical and clinical development program, in which over 20 trials of 1000 patients were performed.

BTG said it has acquired the commercial rights to BGC 9331, and the comprehensive pre-clinical and clinical data package. In a phase II trial in gastric cancer, the drug resulted in an overall objective response rate of 25 percent, the company said.

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**FibroGen Inc.** of South San Francisco said it has received a phase I small business innovation research grant from NCI to develop anti-cancer agents targeting connective tissue growth factor.

The growth factor is a protein implicated in cancers including pancreatic, acute lymphoblastic leukemia, breast, esophageal, and glioblastoma, the company said.

Since CTGF promotes angiogenesis, FibroGen said it would screen a library of antibodies for leads that bind to CTGF and inactivate its angiogenic activity.

CTGF works in concert with other growth factors (e.g., VEGF, TGF-beta) to recruit and activate tissue-remodeling cells, including fibroblasts, endothelial cells, and smooth muscle cells, involved in angiogenesis.

"The antibodies developed in the project could find application in both primary and late-stage treatment of cancer, indicating significant expansion opportunities for our CTGF-based technology in areas in addition to the treatment of fibrosis," said Thomas Neff, CEO of FibroGen.

FibroGen Inc. is privately held.

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**Implant Sciences Corp**. (AMEX: IMX, IMX.WS) of Wakefield, Tx, said it has received a $709,000 grant from NCI to continue development of an brachytherapy plaque for choroidal melanoma.

Under the grant, the company plans to design and manufacture plaques containing Iodine-125 isotopes. The plaques would improve radiation treatment for tumors by eliminating the large dose deviations that can occur.

The company said it would collaborate with the brachytherapy physics team of Memorial Sloan-Kettering Cancer Center, which will provide dosimetry measurements and medical input.

The conformal plaque will be thinner than the existing seeded plaques and should offer less discomfort while concurrently delivering a more effective radiation treatment to the tumor, the company said.

"Since this device should be an improvement over the existing ocular melanoma treatment modality, this may only require a 510(k) FDA clearance before commercial sales can begin," said Anthony Armini, president and CEO.

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**IVAX Corp.** (AMEX: IVX) (LSE:IVX.L) of Miami said it has begun a phase II trial of talampanel for brain cancer at NCI.

Howard Fine, chief of the Neuro-Oncology Branch at NCI, is the principal investigator.

Talampanel blocks the effect of glutamate, the company said. The drug, administered orally, has been well tolerated.

Ivax has expanded a phase II study for refractory epilepsy and a phase II study Parkinson's disease-associated dyskinesia, the company said.



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