THE CANCER LETTER INTERACTIVE

Vol. 27 No. 46
Dec. 14, 2001

Price $295 Per Year

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

Safety Concerns About Saltz Regimen Were Statistical Artifact, ODAC Finds

The FDA Oncologic Drugs Advisory Committee recommended not changing the label of CPT-11, also known as Camptosar (irinotecan hydrochloride injection), for advanced colorectal cancer.

After reviewing all available data on CPT-11, the committee in effect decided that what originally appeared to be an increase in mortality was, in fact, a statistical artifact that resulted from the use of a new adverse events reporting system by one of the cooperative groups.

The agency sought the unusual reexamination of the therapy because

(Continued to page 2)

In Brief:

AACI: von Eschenbach "Wonderful Choice" For NCI Director, Knows How Centers Work

ASSOCIATION OF AMERICAN CANCER INSTITUTES said it "applauds" President Bush's appointment of **Andrew von Eschenbach**, professor of Urology and center director for the Genitourinary Cancers Program at M.D. Anderson Cancer Center, as NCI director.

"I couldn't be more pleased with the selection of Andy von Eschenbach to head the National Cancer Institute," said **John Niederhuber**, president of AACI and director of the University of Wisconsin Comprehensive Cancer Center. "Andy is a wonderful choice. He is a highly respected and outstanding physician, clinical researcher and administrator, who as a cancer survivor himself, understands well the personal burden of cancer."

Niederhuber said that von Eschenbach's long-time tenure at one of the nation's major cancer centers prepares him well to lead the NCI and provides him with a special insight into the challenges cancer centers face in carrying out multidisciplinary and integrated programs of cancer research.

"Andy knows how cancer centers work and that the clinicians and scientists who work at cancer centers require close collaborations and interactions to carry out research," Niederhuber said. "These vital collaborations are not only enhanced by, but are dependent on new communication and informatics technologies, and we look forward to working with Andy to help strengthen these capabilities at AACI member institutions."

Ronald Herberman, AACI immediate past president and director of the University of Pittsburgh Cancer Institute, said von Eschenbach appreciates the importance of making promising new therapies in the form

(Continued to page 7)

New Reporting System Blamed For CPT-11 Alarm

(Continued from page 1)

earlier this year two clinical trials found an apparent elevation in deaths in patients treated with the "Saltz regimen" of CPT-11 and 5-FU/LV (**The Cancer Letter**, May 11, June 22). The deaths occurred in the early treatment cycles. ODAC approved the bolus Saltz regimen and a separate infusional regimen for the indication in March 2000.

After the trials were suspended, the mortality data were examined by three separate panels: an independent review group, CPT-11 sponsor Pharmacia, and FDA staff. After reviewing the original data that led to approval of the Saltz regimen as well as the data from the three examinations, ODAC voted unanimously to maintain the label in its current form.

Richard Pazdur, director of the FDA Division of Oncology Drug Products, said the committee was asked to review the mortality data in order to resolve the concerns about CPT-11. "There was a great deal of controversy, and we needed to conduct a public discussion not only of the cooperative groups trials, but the registration trials and the audits," Pazdur said. "First, we needed to put the deaths reported in the cooperative group trials in the context of the greater clinical trials database. Also, we could not tolerate uncertainty here, because this regimen is widely used as a control arm for trials in colorectal cancer."

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

World Wide Web: http://www.cancerletter.com

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

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
E-mail: news@cancerletter.com

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
E-mail: info@cancerletter.com

Subscription $295 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd

After discussion, the committee left it to FDA staff and the sponsor to discuss potential changes in toxicity management guidelines and dose modifications for the Saltz regimen.

"We've been working with this particular regimen since 1994," Leonard Saltz, a colon cancer specialist at Memorial Sloan-Kettering Cancer Center, said to **The Cancer Letter**. "We've learned some things from experience and from familiarity with it. Now, the agency has the latitude to incorporate this knowledge into treatment guidelines."

FDA's Pazdur cautioned against arbitrary reductions in the doses of CPT-11 and 5-FU. "Such reductions could erode the modest survival advantage demonstrated by this regimen," Pazdur said. "Under the worst-case scenario, the patients would suffer the toxicity without the benefit of a survival advantage."

The Trip Wire

The meeting produced a surprise: Officials of the North Central Cancer Treatment Group said the group's initial findings of elevated mortality last summer didn't justify the change of a label.

The cooperative group originally sounded an alarm as a result of adopting a new system for tracking adverse events from all causes in the cooperative group trials, said Richard Goldberg, chairman of the gastrointestinal cancer programs at NCCTG and at Mayo Clinic.

Goldberg said subsequent examination of the data does not support changing the label of CPT-11. "I've spent a lot of time thinking about this, including time when I wish I were sleeping," Goldberg said at the ODAC meeting Dec. 6. The apparent problem emerged soon after the cooperative group began to use a new method for reporting adverse events. All grade 4 and 5 toxicities were reported to NCCTG.

"The difficulty was that such a type of monitoring system had never been used in phase III trials, and one of the problems was, where do you set the red line?" Goldberg said at ODAC. "What we determined was that if you look back at clinical trials in advanced colon cancer, most reported 1-percent mortality rate related to treatment at any point in the course of therapy. What we found was that when we were reviewing the charts on every patient that died was that investigators often classify it as non-treatment-related. We found out when we went though the charts that [the deaths] were either caused by the treatment, or at least were treatment-exacerbated. And that allowed us to choose a metric that was

independent of what the investigator thought in terms of assigning the mortality within 60 days of the first treatment. It was a metric that we were learning from as we were using it," Goldberg said.

The NCCTG trial compared the Saltz regimen with oxaliplatin and 5-FU/LV and Oxaliplatin and CPT-11.At the time NCCTG sounded alarm, 60-day mortality on the Saltz regimen was 4.8 percent, compared to 1.8 percent on the other arms.

NCCTG set a confidence interval of 95 percent above the 1-percent mortality factor as the red line, Goldberg said. That meant that if the group had more than 3 percent deaths within 60 days, the trial would be suspended. "When we got two additional deaths that brought us up to 13 deaths on the Saltz regimen arm, we had to figure out why that was happening," Goldberg said.

Saltz said the 1-percent trigger used by NCCTG was wrong. Based on historical controls, the anticipated 60-day mortality metric should have been around 7 percent, he said.

"The mortality rate that we were seeing on the two experimental arms was lower, but we don't know whether this survival rate translated into a better survival or activity rate," Goldberg said. "I have become convinced as I thought about it more and more that the conclusion that Pharmacia, and the advocacy groups have come to is the right conclusion, and that is that there is not enough data to say that one of the standard ways of giving CPT-11 and 5FU/LV should no longer be permitted."

However, reviewing the toxicity data has alerted physicians to the possibility that the treatment may be more harmful than helpful to patients who have a poor performance status. "We need to be attentive to patient side effects during the course of therapy," Goldberg said. "It's not permissible to just write, Give four doses, and I will see the patient in six weeks."

Following the NCCTG action, CALGB, too, suspended its trial of the regimen in adjuvant setting, and the investigations of the mortality were launched. One of the investigations, conducted by a panel headed by Mace Rothenberg of Vanderbilt University, was published in the Journal of Clinical Oncology (19:3801, 2001).

Saltz said the ODAC decision puts the controversy to rest. "There was an 'apples and oranges' comparison made between investigator-judged treatment-related mortality, and a new metric, the 60-day all-cause mortality," Saltz said. "There was also a lack of awareness that the 60-day all-cause mortality in most previous metastatic colorectal cancer trials using 5-FU/LV alone had been higher than what was seen with CPT-11/5FU/LV in the NCCTG tral."

ODAC member Kathy Albain agreed. "Since the approval, the data have not changed," said Albain, professor of Medicine at Loyola University Medical Center. "It's just a different way of looking at it. And it also points out just how toxic simple 5-FU can be, as used in this country in many settings still."

Bolus vs. Infusion

The CPT-11 combination was approved for two regimen, the bolus Saltz regimen, and infusional Douillard regimen. In separate studies, the Duillard regimen appeared to cause fewer deaths on protocol within the first 60 days. Comparing the two separate studies, FDA official Robert Temple asked the committee to decide whether the infusional regimen would be preferable to the bolus regimen.

"One could recommend that [the infusional regimen] be considered preferable, if available," said Temple, director of the FDA Office of Drug Evaluation I. "Could you make it clear what the deficiencies are that don't allow you to conclude that the Saltz regimen is toxic, just some clarification, just so we understand the reasoning?"

"The simple answer to that is that they are not head-to-head comparisons," said ODAC member George Sledge, professor of the departments of Medicine and Pathology at the Indiana University School of Medicine. "It's a reasonable hypothesis that infusional 5-FU might be safer than bolus 5-FU, but I don't think any one of us around this table would consider it anything but a hypothesis."

ODAC chairman Stacy Nerenstone said the infusional regimen would be difficult to implement in the U.S. "Dr. Temple, I am sure that you realize how much of a big deal it is to go from a bolus to an infusional setup," said Nerenstone, associate clinical professor at Helen and Harry Gray Cancer Center at Hartford Hospital.

"Yes, there are large institutions that continue to use infusion," Nerenstone said. "But out in the community, it's very hard; not because the doctors don't accept it, but because the patients don't accept it. I think you are trying to fix something that isn't broke."

TEMPLE: "Would you urge the cooperative groups to actually do a head-to-head on CPT-11 given in various regimens?"

NERENSTONE: "That would have to be a very

large trial, because you are talking about a toxicity-reduction trial. So you are talking about tying up a lot of resources and a lot of time without any thought that you are going to move the treatment of metastatic colon cancer forward."

Infusion is particularly impractical at hospitals that serve the poor, said ODAC member Otis Brawley, associate director for cancer control and professor of medicine and epidemiology at Winship Cancer Institute and Emory University School of Medicine. Brawley, a former NCI official, is one of the two newest members of ODAC. Another new member is Stephen George, a Duke University biostatistician.

As Pharmacia and FDA attempt to come up with the guidelines for managing toxicity, they may find it difficult to steer away from interfering with medical judgment, observers said. The studies showed that patients with the performance status of 2 on the ECOG scale did poorly on the Saltz regimen.

Saltz points out that PS 2 patients getting his regimen were not alone in experiencing these problems.

"Underempahasized in the discussion was the fact that both the sponsor and the agency presented data that all PS 2 patients, whether they got the bolus schedule of 5-FU or the infusional schedule, and whether or not they even got CPT-11, did poorly," Saltz said to **The Cancer Letter**. "The cooperative groups have already stopped enrolling PS 2 patient in some lung cancer trials, and many large colorectal trials are doing the same. Clearly, if a warning of any sort regarding PS 2 patients is going to be required, it would seem appropriate to have it in all regimens, and realistically for all treatments in solid tumor oncology, and not specific to one particular schedule in colon cancer.

"In my opinion, such a warning is too broad to be attached to any one drug or any one regimen," said Saltz.

Subjectivity is a hazard in assessing performance status, Pazdur said. "Once a drug gets out there, there are no restrictions on which patients may receive that drug," he said. "The agency does not want to impair sound medical judgment."

In other actions:

—The committee was unable to reach consensus on Gliadel Wafer (polifeprosan with carmustine implant) for the newly diagnosed malignant glioma. Gliadel received marketing approval from the FDA in September 1996 to treat recurrent glioblastoma multiforme. The therapy is sponsored by Guilford Pharmaceuticals.

—The committee voted unanimously 16-0 to recommend including new information to physicians using Herceptin (Trastuzumab) about a gene-detection test called FISH (fluorescence in situ hybridization) (PathVysion) that identifies women with metastatic breast cancer who could benefit from Herceptin.

Herceptin is approved for both first-line therapy in combination with paclitaxel and as a single agent in second- and third-line therapy. FISH is a diagnostic test used to determine the number of HER2 genes in a patient's breast cancer cells.

Women whose cancer cells contain too many copies of the HER2 gene are candidates for Herceptin therapy. Herceptin is designed specifically to block the cancerous growth-promoting products of the excessive number of HER2 genes.

FISH testing measures the number of genes in each cell, using fluorescent dye so the HER2 genes can be visualized and counted with a special microscope. More than the normal two HER2 genes per cell are present in HER2 positive breast cancer.

NCI Notes:

Campus-Dweller Rabson Finds Comfort In NIH Security

The NIH campus has changed dramatically in the weeks since Sept. 11, and few people have felt the effect more than two key officials of the Institutes.

For the past 35 years, Acting NCI Director Alan Rabson and Acting NIH Director Ruth Kirschstein have lived in a house on campus in the shadow of Building 31.

Now in their 52nd year of marriage, the two have worked at NIH for a combined total of 90 years.

After the terrorist attacks on the World Trade Center and the Pentagon, the General Services Administration moved to increase security at all federal buildings. NIH hired guards, closed off all but a few of the roads entering the campus, issued ID cards to employees, and began inspecting vehicles of visitors.

"Our lives at NIH will never be the same," Rabson said to the National Cancer Advisory Board at its Dec. 4 meeting. "NIH in the past has always prided itself on the fact that we have an open campus, not like most federal establishments. We've never had much security."

Rabson said that for the most part, he likes the idea of increased security. "Since my wife and I are

total wards of the government—we live on this campus in a little government house—we've found we actually like the security," he said. "The open campus was wide open, with people wandering around at night. So there is a certain benefit."

On the other hand, the security measures are expensive. "This does cost a great deal out of the NIH budget," Rabson said.

Some visitors complain about the five- to 10-minute vehicle inspection, but Rabson said that he knew of at least one unexpected benefit. A scientist arrived late to a meeting at NCI and explained that the security guards had him open his car trunk and hood, and then they ran a gadget with a mirror on it under the car. Rabson said when the guard was finished with the inspection, he said to the scientist, "Hey, Doc, you got a big hole in your muffler."

Rabson said he told the story at a recent meeting of institute directors. "Steve Katz, director of the arthritis institute, said I am sort of the ultimate Pollyanna and I can find something cheerful about almost anything," Rabson said.

Next on the GSA list is "something called a perimeter fence" around the NIH campus, Rabson said.

The idea of a fence "has sent a shudder through some of the NIH community," he said. "When we have a perimeter fence, which I'm sure is not going to be inexpensive, it could be helpful, because right now, people can just walk onto the campus."

Some days after Sept. 11, Rabson and Kirschstein ordered dinner delivered from their favorite local Chinese restaurant, Rabson said to **The Cancer Letter**. They left instructions for what the delivery person should tell the security guards, and figured the food would be delayed.

To their surpirse, the driver and food arrived quickly. The driver explained that he had simply parked on a street next to the campus and walked up to their house.

When the fence goes up, Rabson and Kirschstein may have to wait longer for their dinner.

* * *

The average term of an NCI director in modern memory—that is, the memory of NCI Acting Director Alan Rabson, who began work at NIH in 1955 and serves as unofficial historian—is 5.75 years, Rabson informed the National Cancer Advisory Board.

"I've been here 46 years," he said. "I've been through eight directors. I did a little quick calculation: eight directors, 46 years, that's 5.75 years for the half-life of a director."

Former director Richard Klausner stayed a little over six years.

Rabson said he sees his eight directors every day, in portrait form, as he zips down the hall of the 11th floor of Building 31 to budget director John Hartinger's office. Upon their resignation, NCI directors are commemorated in large paintings, complete with American flags, some wearing PHS Commissioned Corps uniform, others in lab coat or coat-and-tie.

Rabson, 75, generally spry and quick on his forrays through Building 31, appeared at the NCAB meeting in a wheelchair. He said it was due to a pulled muscle, the result of a struggle with a garage door.

"Of all of my directors, each one is special in my life, but I can say without hurting any of their feelings that Rick is the most brilliant, charismatic, articulate, imaginative, and creative," Rabson said to the NCAB. "Those are the things he brought to that office."

Rabson said when Klausner asked him to serve as deputy director in 1995, he told Klausner that he divided his NIH career into 20-year segments: 1955-75 in the pathology lab; 1975-95 director of the NCI Division of Cancer Biology.

"I told him, 'You'll have to keep me on until 2015,'" Rabson said. "He was a little taken aback by that."

As an acting director, Rabson will not automatically qualify for a portrait when the newly appointed director, Andrew von Eschenbach, arrives next month.

It's doubful that Rabson would sit for a portrait, since he isn't going to retire.

Not "has no plans to retire." Isn't going to.

At least until 2015.

A quick calculation: That's 2.43 more directors.

Probably not even then.

* * *

In fiscal 2001, most of the $442 million in new appropriations that NCI received paid for non-competing research grants, former NCI Director Richard Klausner said at the Sept. 11 meeting of the National Cancer Advisory Board.

The details of Klausner's budget report, hardly the most important news of that day that saw the terrorist attacks on the World Trade Center and the Pentagon, as well as Klausner's resignation, appear in the official minutes of the NCAB meeting:

"Of 442 million new dollars, two-thirds went into

research grant activities, and two-thirds of that went into paying the cost of non-competing grants, which increased by 10 percent over FY 2000. There was a 123 percent increase in competing awards; in the last year, the NCI awarded about 1,200 new and competing grants, an increase of 7.5 percent. The total size of the NCI grant pool last year was $1.7 billion, which is larger than the entire budgets of all but three NIH Institutes.

"A total of about 750 R01 grants were funded, which represents a 5 percent increase in numbers and a 20 percent increase in dollars. The average per-year cost of a grant increased from $299,000 to $340,000. The payline remained in the 22nd percentile.

"The NCI expects to reduce the use of downward negotiation this year because a cap has been placed on increases in the amount that can be requested for P01 and R01 competing renewals. The fact that Type 2 R01s, which are competing renewals, increased an average of 45 percent last year will continue to be a major concern.

"Cancer Centers grew by 18 percent, and the SPORES program grew by 30 percent. The K Awards, a career program, also continues to be a priority. About 400 awardees will be supported with 2001 funds, an increase of about 25 percent. Over the last 2 years, the NCI has nearly doubled the career program.

"Last year, about 7 percent of the dollars available for grants were set aside for new Special Initiatives based on priorities in the Bypass Budget."

For the full text of the Sept. 11 meeting minutes, see: http://deainfo.nci.nih.gov/Advisory/ncab/119_1001/mins11sep01.PDF

* * *

The National Cancer Advisory Board formally recognized former NCI Director Richard Klausner for his service to the Institute.

The resolution was presented to Klausner at the board's Dec. 4 meeting.

The text of the resolution follows:

"Whereas, Dr. Richard D. Klausner, as part of his long and continuing association with the National Institutes of Health that began in the National Cancer Institute in 1979, came to be appointed by the President as Director of the NCI in August of 1995; and,

"Whereas, in that service to the NCI and the American people, Dr. Klausner, through his gifted organizational vision and profound scientific understanding reorganized, revitalized, and raised to new heights the capabilities of the Institute and the National Cancer Program to respond to the challenges and opportunities facing the Nation in its War on Cancer; and,

"Whereas, in all these endeavors his precept of inclusion opened up and brought into the NCI the diverse scientific, advocate, industrial, professional and governmental communities as true colleagues and stakeholders in common in the fight against cancer; and reflected his concern for the people with cancer through the development and growth of initiatives such as the Director's Consumer Liaison Group and Progress Review Groups; and,

"Whereas, he shared and implemented his goal for the NCI Bypass Budget to be an inclusive, understandable blueprint for opportunities and progress that represents to the Congress and the American Public a unified vision of how scientific and medical research can be planned and targeted to assure effective use of public funds; and,

"Whereas, this document has become by acclamation the standard by which a government agency communicates its mission and vision; and,

"Whereas, the many unprecedented research infrastructures that he set in place such as the Cancer Genome Anatomy Project, Cancer Genetics Network, Molecular Target Laboratories, Director's Challenge, Informatics initiatives, Early Detection Research Network, Mouse Models Consortium, and resource programs such as RAID, RAPID and DCIDE have proven many times over their value and flexibility to speed both discovery and its applications to many cancers; and,

"Whereas, Dr. Klausner exemplifies through his own extraordinary dedication, capabilities, and achievements that the call to public service is a noble one that should attract the best and brightest of each generation; and,

"Whereas, he did all of these things, and more, with dedication, energy, intellect, grace, caring, compassion, and humor,

"Therefore, be it resolved that the National Cancer Advisory Board recognizes and honors Dr. Richard D. Klausner for his leadership, vision, and unique contributions which have made the National Cancer Institute the clear and shining beacon of cancer research in the world, an exemplar of what is best about what government can do for the benefit of all people; and the Board is certain that he will continue to use his peerless skills and dedication for the benefit of all as he embarks upon his new career."

The Cancer Letter Takes Winter Publication Break

This issue, Vol. 27, No. 46, Dec. 14, 2001, is the final issue of **The Cancer Letter** for 2001.

The next issue, Vol. 28, No. 1, will be published Jan. 4, 2002.

Happy holidays and a healthy and productive New Year to our readers.

Funding Opportunities:

USP Fellowship Program

Application Deadline: Jan. 31, 2002.

Applications are being accepted for the U.S. Pharmacopeia Fellowship Program. Six fellowships of up to $20,000 each will be awarded.

Applicants must be accepted for full-time study in a Ph.D. program or medical school, a fellowship program, or have a postdoctoral research (nonfaculty) appointment. Any university official or faculty advisor can sponsor the applicant. For application information, see http://www.usp.org/fellows-interns.

Inquiries: Justin Lane, phone 301-816-8323; e-mail Fellows/Interns@usp.org.

2002 USP Summer Internship Program

Applications Deadline: Feb.1, 2002.

Medical, pharmacy, nursing, public health, and international health students in the final two years of accredited programs are encouraged to apply. A stipend of $8,500 is offered for the 12-week program, which begins May 20, 2002, and concludes Aug. 16, 2002.

Inquiries: See preceding entry.

Other Funding Notices

All United States Postal Service mail and courier deliveries for the receipt of additional copies of grant applications (in response to RFAs and PAs) addressed to NCI must be sent to:

Referral Officer, Division of Extramural Activities, NCI, 6116 Executive Blvd., Rm 8041, MSC-8329, Rockville, MD 20852 (express courier), Bethesda, MD 20892-8329.

Applications hand-delivered to NCI will no longer be accepted. This delivery policy does not change any application receipt date requirements for RFAs and PARs. This change in practice is effective immediately.

This policy is similar to and consistent with the policy for applications addressed to Centers for Scientific Review as published in the NIH Guide, http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-012.html.

In Brief:

Cancer Centers Pleased With Bush Choice For NCI

(Continued from page 1)

of clinical trials available to patients as quickly as possible. "We already have begun to work with NCI to develop a public-private mechanism of support to facilitate the testing of novel therapies, and I am delighted at the prospect of working with Andy and his leadership team at NCI to finalize the details of this program," Herberman said.

The AACI, based in Pittsburgh, is an association of the nation's leading academic and freestanding cancer centers.

* * *

MEDICAL COLLEGE OF WISCONSIN International Bone Marrow Transplant and Autologous Blood & Marrow Transplant Registries, in collaboration with the National Marrow Donor Program and the EMMES corp., received a five year, $11 million grant from NIH. The grant enables the groups to serve as a data and coordinating center for a national blood and marrow transplant clinical trials network that will link 14 U.S. transplant program consortia performing blood stem cell transplant therapy. The study sites that will work with the IBMTR and ABMTR include Case Western Reserve University Consortium, Dana Farber Cancer Institute, Duke University, Johns Hopkins University and Sloan-Kettering Cancer Center. . . . **SUSAN G. KOMEN** Breast Cancer Foundation announced the 2001 recipients of its Professor of Survivorship Award: **Carolyn Gotay**, of the Cancer Research Center of Hawaii at the University of Hawaii; and **Ian Tannock**, of the Ontario Cancer Institute/Princess Margaret Hospital, at the University of Toronto. Selected by a committee of peers and breast cancer survivors, each Professor of Survivorship receives $20,000 for use in advancing the field of research specific to the unique medical and psychosocial issues faced by breast cancer survivors. . . . **C. BRUCE TARTER**, director of Lawrence Livermore National Laboratory, will leave his position in 2002. . "For more than 30 years, Tarter has worked to make Lawrence Livermore National Laboratory one of the nation's leading research institutions, first as a scientist and then as a manager," said **Spencer Abraham**, Secretary of the Department of Energy. . . . **NEW JERSEY'S** plan to extend Medicaid benefits to women with breast or cervical cancer through a federal screening program were

approved by the Department of Health and Human Services. New Jersey is the 33rd state to take advantage of the federal Breast and Cervical Cancer Prevention and Treatment Act of 2000, which allows states to expand Medicaid coverage. Under the law enacted last year, states can extend the full Medicaid benefit package to women who were screened through the NBCCEDP run by CDC. Since the program began in 1990, more than 3 million breast and cervical cancer screening tests have been provided to more than 1.8 million women. . . . **CARL D'ORSI** was named program director for oncologic imaging at the Winship Cancer Institute in Atlanta and director of the Division of Breast Imaging in the Department of Radiology at Emory University School of Medicine. D'Orsi will also oversee development and operation of the Avon Breast Center at Grady Hospital, which is being built as part of the Georgia Governor's Cancer Coalition and is the first Center of Excellence designated by Governor Roy Barnes. D'Orsi holds professorships in surgery and pathology at University of Massachusetts Medical Center in Wocester, Mass. He is also professor and vice chairman of the Department of Radiology at the University of Massachusetts Medical Center and lecturer on radiology at Harvard Medical School. D'Orsi is a founder of the Society of Breast Imaging and serves as chairman of the Breast Cancer Task Force of the American College of Radiology. . . . **DOUGLAS PENN**, professor, Department of Oral and Maxillofacial Surgery at University of Florida College of Dentistry, was named editor of the Dentomaxillofacial Radiology journal for a six year appointment. . . . **JEFFREY ESKO**, one of the nation's top researchers in the hot new field of glycobiology the structure, function and metabolism of glycans, the body's array of complex sugars, was elected president of the Society for Glycobiology at its national meeting last month in San Francisco. A professor of Cellular and Molecular Medicine at the University of California, San Diego School of Medicine, Esko is associate director of the UCSD Glycobiology Research and Training Center. Recent advances in glycan studies have encouraged researchers throughout the world to investigate these compounds, which are a major ingredient of every living organism. As varied in structure as they are ubiquitous, glycans are attached as long intricate chains to proteins and fats, or exist freely on their own. They promote communication and connections between healthy cells, and can be deeply involved when things go wrong, for example in infectious disease, inflammation and cancer.

THE CANCER LETTER

Vol. 16 No. 11
December 2001

Business & Regulatory Report

Clinical Trials:

Endostatin Enters Phase II Trial For Neuroendocrine Tumors

EntreMed Inc. (Nasdaq: ENMD) of Rockville, MD, said it has begun a phase II trial of Endostatin for neuroendocrine tumors.

Dana-Farber/Partners CancerCare, a collaboration of Dana-Farber Cancer Institute, Brigham and Women's Hospital and Massachusetts General Hospital, will coordinate the study, which is designed to measure tumor response, the company said. Patients will self-administer Endostatin using pre-filled syringes.

Endostatin received orphan drug status for neuroendocrine tumors

(Continued to page 2)

Oncology Management:

Siemens To Provide Technology To DxTx For Lung Cancer Detection

DxTx Corp. of Mountain View, CA and **Siemens Medical Solutions** (NYSE:SI) of Concord, CA, said the Oncology Care Systems Group of Siemens Medical Solutions has taken an equity position in DxTx.

Under the agreement, Siemens will provide technology resources including computed tomography, positron emission tomography, linear accelerators and oncology management software, the companies said. DxTx will integrate the Siemens Seek-Find-Act-Follow approach to disease state management into its proprietary cancer solution platform. The companies said their goal is to improve the prognosis for lung cancer while making screening and early diagnosis available to the public for those at high-risk

DxTx will create freestanding outpatient centers using an end-to-end integration of screening, diagnosis, treatment and follow-up, the company said.

The non-invasive approach uses proprietary technologies developed by DxTx and its partners in the areas of computer-assisted detection 3D inverse treatment planning, utosegmentation, respiratory gating and intensity modulated radiation therapy, the company said.

* * *

OnCure Technologies Corp. (OTCBB:ONCU) of Oakdale, CA, said it has signed a renegotiated medical service agreement with the **Johnson Tepperman Medical Group Inc.** to provide radiation oncology services for the OTC comprehensive cancer center in Stockton, CA.

In addition, OTC approved contracts with community payors **Medcore IPA** and **Delta IPA**, the company said. Medcore IPA, operating

(Continued to page 8)

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

EORTC Begins Phase I/II Trial Of Halofuginone

(Continued from page 1)

earlier in the year, the company said.

* * *

Collgard Biopharmaceuticals Ltd. and the **European Organization for Research and Treatment of Cancer** said they have begun enrollment in a phase I/II trial of Halofuginone tablets for advanced-stage cancer.

The study, an open-label, dose-escalation study using once-a-day oral administration, will take place in two centers in Europe: Rotterdam, The Netherlands and Leuven, Belgium, the company said.

The trial endpoints are safety and identification of clinical effects to the mechanism of action, the company said. Halofuginone affects tumor growth by a combination of distinct inhibitory mechanisms—termed Panstasis—that inhibits tumor stromal support, angiogenesis, invasiveness and cell proliferation.

The study will also address an extensive translational research program in collaboration with the EORTC Pharmacology and Molecular Mechanisms Group," said Pierre Fumoleau, chairman of EORTC/ECSG.

An earlier double-blind, placebo-controlled dose finding phase I study was conducted in healthy volunteers, the company said. PK results indicated high bioavailability of the drug in humans and a long half-life. In addition, the drug was found not only to yield plasma levels within the dose range of those attained in animal efficacy models, but was also identified in body fluids mainly unchanged, the company said.

* * *

Genaera Corp. (Nasdaq: GENR) of Plymouth Meeting, PA, said it has begun a phase IIB trial designed to test squalamine, an angiogenesis inhibitor, for non-small cell lung cancer.

The multi-center randomized study will evaluate up to 90 patients receiving weekly dosing of squalamine, combined with weekly chemotherapy of carboplatin and paclitaxel, in stage IIIB or stage IV advanced disease, the company said. Half of the patients will receive a dose of 100 mg/m2, and the other half will receive a dose of 200 mg/m2. The optimization in dosing regimen could yield an improved safety and efficacy profile for the combination of squalamine and the chemotherapy agents.

Earlier this year, Genaera announced results from its phase IIa trial in NSCLC, examining the preliminary efficacy and safety of the inhibitor, combined with carboplatin and paclitaxel, the company said. Objective responses were observed in 29 percent of patients (9 of 31), receiving the treatment dose of squalamine (300 mg/m2/day) for one or more cycles of therapy. Overall, 27 percent (12 of 45) experienced an objective response. The median survival time is now determined for the first 18 patients in the study, which was the dose escalation portion, as 10.4 months, the company said. The historical benchmark objective response rate for this group treated with carboplatin and paclitaxel alone is 15 percent, with 8.2 months survival, as demonstrated in the large Eastern Cooperative Oncology Group study.

* * *

Gilead Sciences Inc. (Nasdaq:GILD) of Foster City, CA, said it has initiated the first phase I trial of GS7904L, an investigational liposomal thymidylate synthase inhibitor for solid tumors refractory to standard therapy, in Germany.

Additional trials are planned in other countries in the coming months, the company said.

The trial is designed to evaluate the safety, tolerability and toxicity of the inhibitor in up to 40 patients at two sites, the company said. The dose of GS7904L will be escalated in successive cohorts to determine the maximum tolerated and recommended phase II doses.

GS7904L is a thymidylate synthase inhibitor

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

World Wide Web: http://www.cancerletter.com

Business & Regulatory Report

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

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
E-mail: paul@cancerletter.com

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

belonging to the same class of agents as the 5-fluorouracil (5-FU). GS7904L has demonstrated activity in a variety of preclinical cancer models including colorectal, ileocecal and ovarian cancers, the company said.

In another development, Gilead and **OSI Pharmaceuticals** (Nasdaq:OSIP) said they have signing of an agreement for OSI to acquire the Gilead pipeline of clinical candidates in oncology and the Gilead Boulder, CO, operations, including clinical research and drug development personnel and infrastructure.

OSI will pay $130 million in cash and $40 million in shares of its common stock upon the closing of the transaction, the company said. OSI will also pay Gilead up to an additional $30 million in either cash or a combination of cash and OSI common stock upon the achievement of certain milestones.

Under the transaction, OSI will receive exclusive worldwide development and commercialization rights to three Gilead investigational oncology agents, including GS7904L, the company said. The two additional product candidates are NX211 (liposomal lurtotecan), a proprietary liposomal formulation of the active topoisomerase I inhibitor lurtotecan, in phase II trials for solid tumors; and GS7836, a nucleoside analogue, which is in phase I trials for refractory solid tumor xenograft models.

The transaction is expected to close by year-end., the company said.

* * *

GlycoDesign Inc.(TSE:GD) of Toronto said it has begun the expanded phase II trial program of GD0039 for metastatic renal cancer at the Institut Gustave Roussy in Paris.

The University of Chicago and the Cleveland Clinic are screening patients for entry into the North American metastatic renal trial, ONC-B4.

Each trial will consist of 27 patients. GD0039 will be taken orally twice a day with an evaluation after eight weeks of treatment, the company said. The company said results from both of the trials could be in by the end of 2002.

GD0039 is an orally administered anti-cancer drug that blocks the production of specific carbohydrates that coat the outside of cancer cells, the company said. Studies indicate that GD0039 also stimulates the immune system and has fewer side effects.

* * *

Lorus Therapeutics Inc. of Toronto said it has initiated a phase III trial of Virulizin for advanced pancreatic cancer.

The double-blind, randomized trial will be conducted at 40 North American medical centers for 350 patients, the company said. Patients will be randomized to receive either treatment with gemcitabine or treatment with gemcitabine in combination with Virulizin. Patients who fail or become refractory to gemcitabine will be treated with 5-Fluorouracil or with 5-FU in combination with Virulizin. All study subjects will be monitored throughout the remainder of their lifespan, the company said.

Virulizin is approved in Mexico for malignant melanoma, the company said.

The company said it had struck a seven-year sales and distribution agreement for Mexico, which provides Lorus with an opportunity to receive its first revenue from the sale of one of its products. Lorus will receive royalties from the sales of Virulizin and will be responsible for its manufacturing.

* * *

OSI Pharmaceuticals Inc. (Nasdaq: OSIP) of Melville, NY, said **Roche**, its global partner, has initiated a phase III trial of Tarceva (OSI-774) in combination with gemcitabine/cisplatin for non-small cell lung cancer.

Tarceva is a small molecule, anti-epidermal growth factor receptor drug candidate that has demonstrated anti-cancer activity in single agent, open label phase II studies in NSCLC, head and neck cancer and ovarian cancer, the company said. The drug is being developed as a three way alliance between OSI, Genentech and Roche.

The multi-center, 1,000 patient study, is one of two randomized, controlled trials to be conducted by the alliance, the companies said. The study has improvement in patient survival as the primary end-point.

Genentech began the second phase III front-line combination study combining Tarceva with carboplatin (Paraplatin) and paclitaxel (Taxol) in July, the company said.

OSI also said it has begun a phase 1b trial, conducted by Roche, evaluating Tarceva in combination with docetaxel and capecitabine (Xeloda) for advanced breast cancer, which has relapsed after chemotherapy treatment.

* * *

Protein Design Labs Inc. (Nasdaq: PDLI) of Fremont, CA, said it would file a biologic license

application as a result of a phase III trial of Zamyl (SMART M195) for acute myeloid leukemia.

The trial compared treatment with the antibody plus a standardized chemotherapy regimen to treatment with chemotherapy alone where there was failure to achieve complete remission with initial therapy, or where there had been a relapse within one year of achieving complete remission, the company said. Zamyl increased the overall response rate to 43 percent in the Zamyl plus chemotherapy (n=94) from 26 percent in the chemotherapy alone patients (n=97)(p=0.015), when all evaluable patients were analyzed on an intent-to-treat basis.

Zamyl is a humanized antibody that binds to the CD33 antigen on myeloid leukemia cells, the company said. It is the humanized version of the murine M195 monoclonal antibody, licensed by PDL from Memorial Sloan-Kettering Cancer Center in 1989.

Deals & Collaborations:

Myriad In Partnership To Market Products

Laboratory Corporation of America Holdings (NYSE: LH) of Burlington, NC, and **Myriad Genetics Inc.** (Nasdaq: MYGN) of Salt Lake City announced a partnership to make Myriad's predictive medicine products broadly available to primary care physicians in the US.

Under the agreement, LabCorp becomes Myriad's exclusive sales and distribution partner, marketing the products through its 600-person U.S. sales force, the companies said. Myriad will also continue to market its products to oncologists through its own 85-person oncology sales force. All of Myriad's predictive medicine products are included in this new agreement, including the Company's three cancer predictive and its hypertension predictive products.

The Myriad predictive medicine products are to be marketed nationally to LabCorp's more than 200,000 physician customers. Myriad will perform the comprehensive DNA sequence-based tests at its high-capacity molecular diagnostics facility in Salt Lake City. These tests are performed to assess an individual's risk of developing hypertension and cancer, including breast cancer, ovarian cancer, colon cancer, uterine cancer and melanoma skin cancer, the companies said.

The agreement enables LabCorp to provide single-source access to a full complement of products ranging from disease predisposition to diagnosis and monitoring treatment. LabCorp may also enhance their product range by adding specific mutations discovered by Myriad to their screening panels that assess risk of developing disease.

* * *

AnorMED Inc. (TSE:AOM) of Vancouver said that **AstraZeneca** intends to discontinue development of ZD0473 and return all rights for the product candidate to AnorMED.

Results from clinical ovarian and lung cancer studies, where platinum based therapy has failed, indicate the drug does not meet the differentiated profile required by AstraZeneca, particularly in overcoming platinum resistance, the company said. Data from ongoing phase I and II studies in a variety of tumors support the conclusion that ZD0473 is an active drug with a manageable toxicity profile.

AnorMED said it will be evaluating the development options for ZD0473 as an intravenous and oral formulation to maximize partnering opportunities.

A phase II trial for AMD-3100 in stem cell mobilization, supporting its potential in stem cell transplantation should begin next year, the company said.

ZD0473 demonstrated anti-tumor activity including confirmed responses with mono and combination therapy in tumors for cancer including pancreatic and hormone resistant prostate cancer, among others, the company said. The drug has a manageable toxicity profile and it has not been associated with clinically significant neuro- or nephrotoxicity.

* * *

BioNumerik Pharmaceuticals Inc. of San Antonio and **The Cancer and Leukemia Group B** said they have formed an alliance to use advanced information technology to improve the performance of clinical trials data and information management.

An objective of the alliance is the modeling, design and implementation of clinical trials systems and software to enhance the conduct of clinical trial data and information collection, management and analysis, the groups said. BioNumerik will use its computer software programming, development and resources to creation, optimize and implement software for clinical trials in oncology. CALGB is providing its expertise in oncology clinical trials data management and operations as well as testing and implementing earlier versions of the software, the groups said.

BioNumerik and CALGB said they should complete the initial development tasks for the project by the end of the year.

An additional objective is the provision by CALGB of data management and support for two U.S. phase III trials for the BioNumerik proprietary compound designated as BNP7787, the groups said. The compound protects against many of the common and serious toxicities, such as nerve damage and kidney toxicity, associated with existing cancer therapies.

BioNumerik also has a U.S. phase III trial of BNP7787 with paclitaxel, the company said. The study is designed to evaluate the use of BNP7787 to prevent or reduce the incidence or severity of paclitaxel-associated nerve damage.

"The alliance with CALGB is part of our strategy of integrating pharmaceutical technical and business operations in the creation and deployment of high performance information technologies in pharmaceutical research and development," said Frederick Hausheer, chairman and CEO of BioNumerik. "This approach to oncology clinical trials will enhance and streamline communications between experts involved in different operations and locations."

"CALGB is strongly committed to improving cancer care and using the cutting edge of technologies that can help us to perform clinical research more effectively," said Richard Schilsky, CALGB group chair and associate dean for clinical research in the Biological Sciences Division at the University of Chicago.

* * *

Boehringer Ingelheim International GmbH of Ingelheim, Germany, and **ImmunoGen Inc.** (Nasdaq: IMGN) of Cambridge, MA, said they would collaborate on the development on a product combining the ImmunoGen maytansinoid tumor-activated prodrug technology with a Boehringer Ingelheim antibody.

Under the agreement BI will receive exclusive worldwide rights to commercialize maytansinoid TAPs using antibodies targeting CD44, the companies said. The company will be responsible for the manufacturing, product development and marketing of products resulting from the license. ImmunoGen will manufacture preclinical and initial clinical materials for manufacturing payments, the companies said. ImmunoGen will receive an up-front payment and milestone payments, in addition to royalties on net sales.

Financial terms were not disclosed.

* * *

Exelixis (Nasdaq: EXEL) of South San Francisco and **Bristol-Myers Squibb** (NYSE: BMY) have identified and selected the first small molecule cancer targets in their new collaboration using Exelixis' proprietary screening platform to identify novel targets to combat cancer, the companies said.

The pool of targets come from genome-wide screens to identify genes that functionally interact with the p53 tumor suppressor in Drosophila (the fruit fly) and C. elegans (a laboratory worm). In conducting that screen, Exelixis has identified new strategies by which tumor cells evade normal growth control mechanisms. Mutations in p53 have been implicated in more than half of human cancers, including cancer of the breast, lung, colon, and liver. The cancer targets discovered by Exelixis will now advance into small molecule drug discovery programs at both companies with a goal of identifying novel anti-cancer agents.

In July 2001, Exelixis established a broad collaboration and licensing agreement with Bristol-Myers Squibb to create a new generation of potential cancer drugs that selectively destroy cancers that harbor defects in tumor suppressor gene pathways. Exelixis will identify and validate various molecular targets that trigger cell death in cancer cells while leaving normal cells unharmed. Each company has the option to obtain worldwide rights to equal numbers of validated targets arising from the collaboration. Under the agreement, Exelixis received an exclusive worldwide license to develop and commercialize a specific analogue of the BMS compound, DEAE Rebeccamycin, which has completed phase I safety trials and is currently in phase II clinical trials with NCI. Under the agreement, BMS made an equity investment in Exelixis, paid an up-front licensing fee and continues to provide research support to Exelixis.

* * *

Celgene Corp. (Nasdaq: CELG) of Warren, NJ, said it has signed agreements with **Pharmion Corp.** and **Penn Pharmaceutical Services Ltd.** to expand its Thalomid (thalidomide) franchise internationally.

The European presence of both Pharmion and Penn, combined with Penn FDA-compliant manufacturing capability and the Pharmion global development and marketing expertise, will strengthen the strategy to establish Thalomid in the international markets, the company said.

Under the agreements, Celgene has granted Pharmion exclusive licenses to its intellectual property

covering thalidomide and S.T.E.P.S., the system for thalidomide education and prescribing safety, as well as preclinical and clinical data for international regulatory filings in exchange for royalties, the company said. Separately, Celgene said it has obtained an option to acquire an equity stake in Pharmion.

Celgene also acquired an exclusive option to purchase Penn T, the branch of Penn Pharmaceutical Services that manufactures the drug, the company said. If exercised, the option would enable Celgene to receive a 36 percent royalty on all Thalomid sales including cost of goods sold and manage the manufacturing of the drug as a wholly owned subsidiary of Celgene. Celgene retains the rights for the drug in North America, China, Japan, Korea, and Taiwan, the company said.

In another development, Celgene Corp. and the **Joan and Sanford I. Weill Medical College of Cornell University** said data from an in vitro study determined that thalidomide and IMiDs inhibited COX-2 (Cyclooxygenase-2).

Based on these data, the companies have expanded their research partnership to a three-year collaboration to evaluate the molecular mechanism by which thalidomide and IMiDs regulate COX-2 expression, the companies said.

COX-2 plays a role in promoting inflammation and angiogenesis while inhibiting immune response and apoptosis, the companies said. Recent studies suggest that COX-2 may be in the maintenance of tumor viability, growth and metastasis.

In the study, conducted at Weill Cornell by Andrew Dannenberg, and colleagues, a macrophage cell line was treated with either LPS or LPS and thalidomide, the companies said. Treatment with LPS caused an increase in the amount of COX-2; however, treatment with thalidomide caused a dose-dependent suppression of this effect. IMiDs also inhibited LPS-mediated induction of COX-2.

The three-year research collaboration will evaluate how thalidomide and IMiDs decrease the stability of COX-2 mRNA and determine if the compounds decrease TNF-alpha mRNA by a similar mechanism, the companies said. An additional goal of the partnership is to identify the molecular targets that cause the reduction of COX-2 levels.

* * *

Cell Genesys Inc. (Nasdaq: CEGE) of Foster City, CA, and the pharmaceutical division of **Japan Tobacco** said they would modify their collaboration for Gvax cancer vaccines.

The 50/50 worldwide profit sharing arrangement has changed to a royalty arrangement on sales of Gvax and other cancer indications derived from the vaccine, the companies said. Cell Genesys will have full commercial rights to Gvax prostate cancer vaccine, the companies said.

Under the new agreement, JT will pay CG an undisclosed royalty on the lung cancer vaccine sales in Japan, Taiwan and Korea, and Cell Genesys will pay JT the same royalty on such sales in North America and elsewhere, the companies said.

The companies will continue to equally share in the development costs of the lung cancer vaccine products, and JT will continue to pay Cell Genesys milestone payments, the companies said.

Cell Genesys said it expects no impact on near term revenues relating to this deal modification.

The cancer vaccines are comprised of tumor cells that have been irradiated and genetically modified to secrete GM-CSF, a hormone which stimulates the immune response to vaccines, the companies said. The vaccines have demonstrated antitumor effects against every type of human cancer against which they have been tested to date and are being evaluated in five types of cancer — lung, prostate, pancreatic, leukemia and myeloma.

In a related development, Cell Genesys said it has begun a multicenter phase II trial of the Gvax vaccine for acute myelogenous leukemia.

The trial, to be conducted in the U.S., will evaluate the safety and efficacy of the vaccine in combination with bone marrow transplantation in 50 patients with newly diagnosed AML, the company said. Preclinical data demonstrate the vaccine in combination with bone marrow transplantation prevents relapse of leukemia and increased the overall survival.

* * *

Exelixis Inc. (Nasdaq: EXEL) of South San Francisco and **Genomica Corp.** (Nasdaq: GNOM) of Boulder have signed a definitive agreement whereby Exelixis will acquire Genomica in a stock-for-stock transaction valued at $110 million.

The transaction has been structured as an offer for 100 percent of the Genomica outstanding common stock to be followed by a merger of Genomica with a wholly-owned subsidiary of Exelixis, the companies said.

The offer period will run for 20 business days and, subject to regulatory review, is expected to close at the end of the year, the companies said. The back-

end merger will be completed during the first quarter of 2002. T

The transaction has been unanimously approved by the Boards of Directors of both companies, and the directors, officers and certain affiliates of Genomica have agreed to tender their shares in the offer, the companies said.

* * *

Millennium Pharmaceuticals Inc. (Nasdaq: MLNM) of Cambridge, MA, and **Targeted Diagnostics and Therapeutics Inc.** of West Chester, PA, said TDT has granted Millennium license to the intellectual property of guanylyl cyclase C (GC-C), a protein expressed on the cell surface of colorectal tumors, and its related ST ligand for colorectal cancer therapeutics.

Millennium said it would develop both toxin and antibody-based therapeutics for colorectal cancer.

Under the agreement, Millennium will pay milestone fees and royalties to TDT. Millennium will make an initial equity investment in TDT, the companies said.

GC-C is a receptor that is expressed in metastatic colorectal tumors, but not normal tissues outside the intestine, the companies said.

* * *

OncoGenex Technologies Inc. of Vancouver, B.C., and **Isis Pharmaceuticals Inc.** (Nasdaq: ISIP) of Carlsbad, CA, said they have established a drug development collaboration to co-develop and commercialize OGX-011, an anti-cancer antisense drug candidate for prostate cancer.

OGX-011 combines the OncoGenex proprietary antisense position in inhibitors to the target, clusterin, with the Isis proprietary second-generation antisense chemistry, the companies said. The drug candidate is designed to inhibit the secretory protein clusterin, which acts as a cell-survival protein that is over-expressed in response to tumor killing strategies, such as chemotherapy, hormone ablation and radiation therapy. Clusterin is over-expressed in prostate, renal, bladder, lung, ovarian and urothelial cancers, the companies said.

In preclinical animal studies, OGX-011 improved the potency of traditional chemotherapies more than 10-fold in prostate cancer without compromising safety, the companies said. It has also been shown to reduce levels of clusterin, as well as delaying disease progression in prostate and renal tumor models in animals.

Isis will conduct preclinical toxicology and pharmacokinetic studies and will manufacture OGX-011 for preclinical and phase I/II studies, the companies said. OncoGenex will perform phase I/II safety and efficacy trials of the drug as a single agent and in combination with docetaxel in localized and hormone refractory prostate cancer. **Aventis Pharma Inc.** will provide financial support as well as supply the neo-adjuvant hormone therapy for the study protocol, the companies said.

Specific financial terms of the deal between Isis and OncoGenex were not disclosed, the companies said.

* * *

Prescient NeuroPharma Inc. (CDNX: PRE) of Toronto said it has entered into a letter of intent to license its proprietary anti-cancer compound, Anhydrovinblastine, to **Access Oncology Inc.** of New York.

Prescient will license to Access Oncology exclusive rights to develop and market AVLB, with the exception of Latin America and the Far East, the company said. Including development costs, the parties value the deal in excess of $25 million plus royalties.

The LOI provides for AO to make up-front payments of $1.25 million, milestone payments of $17.5 million, pay royalties on net sales of AVLB and fund all further development of AVLB, including the completion of phase II and phase III clinical trials.

AVLB, a third generation chemotherapeutic, completed a phase I, single center, open label, non-randomized, dose finding safety and tolerance study, the company said. Based on its mechanism of action and pre-clinical data, AVLB may have utility for breast, non-small cell lung, cervical and colon cancer as well as non-Hodgkin's lymphoma, representing a market opportunity well in excess of $500 million, the company said.

* * *

Wyeth-Ayerst Laboratories of St. Davids, PA, the pharmaceutical division of **American Home Products Corp.** (NYSE: AHP) said it has entered into an exclusive option and license agreement with the **Ludwig Institute for Cancer Research** for an anti-cancer LICR antibody therapy.

Under the agreement Wyeth-Ayerst said it could research, develop, manufacture, and commercialize antibody-based drug conjugates and will assume responsibility for the costs. In addition, the company will pay LICR undisclosed option fees, development and approval milestone fees, and royalties on sales of any products.

Oncology Management:

Oncure Renegotiates Agreement With Provider

(Continued from page 1)

exclusively in San Joaquin County, has 150 physician providers and over 22,000 enrolled members. The new contract and relationship with Medcore could increase patient referrals by over 120 patients annually.

Delta IPA, which serves San Joaquin County and the Tracy area has over 200 physician providers and over 80,000 enrolled members, resulting in an additional 12-15 referrals a month, the company said.

"With this agreement, 61 percent of the Oncure net revenue will come from centers with medical service agreements under the earnings model," said Shyam Paryani, chairman of Oncure. "Under the earnings model, Oncure compensates the physician groups after all operating costs. In practices that have historically maintained the earnings model proves to better align the interests of both the practices and the company, with significant increase in practices involvement in local management and community activities."

* * *

Latitude360, the eLearning and eBusiness Solutions division of RWD Technologies Inc. (Nasdaq: RWDT) of Baltimore said **Memorial Sloan-Kettering Cancer Center** has implemented Latitude360's comprehensive eLearning solution, University360. The first course trains management staff on their Annual Performance Appraisal process.

* * *

Precyse Solutions of King of Prussia, PA, signed a long-term contract to provide oncology data management abstracting support to the **Medical College of Virginia Hospitals** of the Virginia Commonwealth University Health System. The contract, which expands Precyse's three-year relationship with MCV, also includes the placement of a full time Cancer Data Manager. This is the third contract win announced by Precyse Solutions in the fourth quarter of this year in the area of ODM services.

Precyse Solutions' oncology team of Certified Tumor Registrars will assist MCV with the collection and management of its cancer data, preparations of its upcoming American College of Surgeons survey and maintaining compliance of its cancer program with Commission on Cancer standards, the company said.

The MCV cancer data will be collected and reported to the regulatory bodies.

* * *

SciFor Inc. of Brewster, NY, said it would archive and offer online access for scientific, technical and medical posters presented at meetings and conferences.

Called E-Poster, the service gives researchers access to posters in the scientific community via the Internet, the company said E-Posters can be accessed and viewed on the SciFor Web site after each author's conference presentation using an individual assigned poster identification number. Each researcher controls access to his or her work by forwarding the number to interested parties at his or her discretion.

Product Approvals & Applications:

Computer-Aided Detection Approved For Mammograms

CADx Medical Systems of Basingstoke, England, a subsidiary of **Shire Pharmaceuticals Group plc** (LSE: SHP.L, Nasdaq: SHPGY, TSE: SQ) said it has received pre-market approval from the U.S. FDA for its second look computer-aided detection system for mammography.

The system consists of a screening tool that provides radiologists with a computerized second review of mammograms, the company said. The system utilizes a technology to highlight areas of concern on a Mammagraph report,

* * *

Cell Therapeutics Inc. (Nasdaq: CTIC) of Seattle said Trisenox (arsenic trioxide) injection has been granted FDA orphan drug designation for both chronic myeloid and acute myelocytic leukemias.

CTI said it is studying the drug as a single agent and in combination with Gleevec for CML in chronic, accelerated and blast crises. In addition, NCI is sponsoring phase II trials for AML.

* * *

NeoPharm Inc. (Nasdaq: NEOL) of Lake Forest, IL, said was granted orphan drug status from FDA for IL13-PE38, its novel tumor-targeting agent for malignant glioma.

NeoPharm said it has exclusively licensed IL13-PE38 from NCI and FDA, and is developing the compound under a cooperative research and development agreement with FDA.

* * *

SuperGen Inc. (Nasdaq: SUPG) of Dublin, CA, said it has received FDA approval to market daunorubicin for a variety of acute leukemias.

Copying Policy for The Cancer Letter Interactive

The software that comes with your issue allows you to make a printout, intended for your own personal use. Because we cannot control what you do with the printout, we would like to remind you that routine cover-to-cover photocopying of The Cancer Letter Interactive is theft of intellectual property and is a crime under U.S. and international law.

Here are guidelines we advise our subscribers to follow regarding photocopying or distribution of the copyrighted material in The Cancer Letter Inc. publications in compliance with the U.S. Copyright Act:

What you can do:

--Route the printout of the newsletter to anyone in your office.

--Copy, on an occasional basis, a single story or article and send it to colleagues.

--Consider purchasing multiple subscriptions. Contact us for information on multiple subscription discounts.

What you can't do without prior permission:

--Make copies of an entire issue of the newsletter. The law forbids cover-to-cover photocopying.

--Routinely copy and distribute portions of the newsletter.

--Republish or repackage the contents of the newsletter.

We can provide reprints for nominal fees. If you have any questions or comments regarding photocopying, please contact Publisher Kirsten Boyd Goldberg, phone: 202-362-1809, email: kirsten@cancerletter.com

We welcome the opportunity to speak to you regarding your information needs.

Click Here for
Photocopying Guidelines