THE CANCER LETTER

Vol. 30 No. 22
May 28, 2004

FDA Approves A New Cancer Drug, Vidaza, And Two sNDAs Without Going To ODAC

By Paul Goldberg

FDA on May 19 approved one new cancer drug and two additional uses for previously approved oncology drugs.

The agency approved a New Drug Application for Vidaza (azacitidine for injectable suspension) for all subtypes of myelodysplastic syndrome. The regular approval was based on response rates, supported by reduction or elimination of dependence on transfusions. The agent is sponsored by Pharmion Corp. (Nasdaq: PHRM) of Boulder, Colo.

The two supplemental NDAs are:

--Taxotere (docetaxel for injection) for use in combination with

(Continued to page 2)

In Brief:

Larry Norton Wins ASCO's Karnofsky Award; Einhorn To Receive ASCO Service Award

LARRY NORTON, deputy physician in chief of Breast Cancer Programs at Memorial Sloan-Kettering Cancer Center, was named the recipient of the David A. Karnofsky Memorial Award, the highest scientific award given by the American Society of Clinical Oncology.

Norton will receive the award and present the Karnofsky Memorial Lecture on June 5 at the ASCO annual meeting, in New Orleans. The title of Norton's lecture is "Ignorato Motu, Ignoratur Natura (Being Ignorant of Motion is Being Ignorant of Nature)."

Norton, a breast cancer specialist, pioneered the "dose density" approach to therapy, which reduces toxicity while maximizing the rate of cancer cell death, but also reduces mortality. As coauthor of the Norton-Simon Model, he has broadly influenced cancer treatment and research for more than 25 years. Norton is president of the National Alliance of Breast Cancer Organizations and was appointed by President Bill Clinton to serve on the National Cancer Advisory Board. He also serves as chairman of the ASCO Foundation Board of Directors and was elected president of ASCO from 2001-2002.

Other recipients of ASCO's Special Awards include:

Lawrence Einhorn, distinguished professor and senior cancer research investigator at Indiana University, will receive ASCO's Distinguished Service Award for Scientific Achievement in recognition of his significant contributions to oncology, including the development of a curative treatment for testicular cancer. Einhorn is internationally renowned for his role in developing a chemotherapy regimen for testicular cancer that has

(Continued to page 7)

A Date With ODAC May Signal Weak Case For Drug Approval

(Continued from page 1)

prednisone for the treatment of metastatic, androgen-independent (hormone refractory) prostate cancer. The agent is sponsored by Aventis Pharmaceuticals Inc. (NYSE: AVE) of Strasbourg, France.

-- Gemzar (gemcitabine HCl) in combination with paclitaxel for the first-line treatment of metastatic breast cancer after failure of prior anthracycline-containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated. The agent is sponsored by Eli Lilly and Co. (NYSE: LLY) of Indianapolis.

The three therapies were approved weeks before regulatory deadlines, and without going to the Oncologic Drugs Advisory Committee. The approvals confirm the observation that in recent years the agency has consulted the advisory group only in cases where applications raise clinical or methodological questions, as well as on theoretical matters, including discussion of endpoints for approval of cancer therapies.

Of the 30 most recent applications accepted by FDA, only six went to ODAC, and three of the six were approved. In 2002, the committee voted down a supplemental indication for Casodex, and earlier this month it recommended against approval of two NDAs, Genasense and RSR13 (**The Cancer Letter**, May 7). The three agents that went to ODAC and received approval were Zometa, Iressa, and Bexxar.

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

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
Letters to the Editor are accepted at the above address.

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
FAQ: Visit www.cancerletter.com

Subscription $315 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

The trend appears to extend to drugs and biologics. Seven of the 30 applications were for biologics. Only one of them, Bexxar, went to ODAC. Two biologics approved so far this year—colorectal cancer therapies Avastin and Erbitux—didn't go to ODAC (**The Cancer Letter**, March 5). Avastin, sponsored by Genentech Inc., was a slam-dunk case, since the agent produced a survival advantage in advanced colorectal cancer.

With the original, unsuccessful, Erbitux application, getting on the ODAC schedule was portrayed as a best-case scenario by the sponsor, ImClone Systems Inc. After ImClone produced new data, the agency approved the monoclonal antibody without consulting the advisory committee.

This means that a date with ODAC—an event that usually drives up the price of a company's stock—could, in fact, be viewed as a sign of problems with the application, an instruction to go to Door No. 2, which is reserved for problem cases. Based on recent data, the probability of an agent squeaking through the committee equals the probability of failure.

While this observation contradicts conventional wisdom on Wall Street, some stock analysts have caught on. "FDA panel review of an oncologic drug indicates a problem with the application, so it's a negative, not a positive," said David Hines, president and director of research at Avalon Research Group of Bocca Raton, Fla., an independent research firm that has an expertise in short-selling. "We were saying that Pharmion's Vidaza was not going to have a problem, because they were not scheduled for a panel. That was a positive. That was certainly not the consensus view. We could be entering a period where it makes sense to sell a stock going to a panel rather than to buy."

For a publicly traded company, an unsuccessful date with ODAC is likely to lead to class action suits. This is the case with Genta Inc., sponsor of Genasense, and Allos Therapeutics Inc., sponsor of RSR13.

Such complaints usually allege that the defendants violated securities laws by issuing "materially false and misleading statements" that inflated the price of their securities.

Vidaza Approval

The Vidaza approval was based on a multi-center, randomized trial in 191 patients with five subtypes of myelodysplastic syndromes, comparing azacitidine treatment to observation only, and in two multi-center single-arm azacitidine trials in 120 patients, the agency said.

The MDS subtypes included in the label are:

refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMMoL).

Vidaza was administered at a dose of 75 mg/m2/day for 7 days every 28 days subcutaneously in the randomized trial and in one of the single-arm trials. Patients in the observation-only arm of the randomized trial were permitted to cross over to Vidaza treatment.

Greater than 50% of observation-only patients crossed over to Vidaza at the time of disease progression. Patients with an adjudicated diagnosis of AML at baseline were excluded from the efficacy analysis of response rate.

Clinical response (complete and partial) was observed in approximately 16% of the Vidaza patients, the company said.

The response rates were similar in patients randomized to Vidaza treatment (15.7%), in patients who crossed over from the observation arm to Vidaza treatment (12.8%), and in patients in the two single arm trials (12.7% and 19.1%). None of the patients in the observation only arm had clinical response. The difference in response rates between Vidaza treated patients and "observation only" patients was statistically significant ($p<0.0001$).

Patients responding to Vidaza had a decrease in bone marrow blasts percentage, or an increase in platelets, hemoglobin or white blood cells. Greater than 90 percent of the responders initially demonstrated these changes by the fifth treatment cycle. All patients who had been transfusion dependent became transfusion independent during complete or partial response.

The mean and median duration of clinical response for patients experiencing complete or partial response was estimated at 512 and 330 days, respectively. Seventy- five percent of the responding patients were still in partial response or better at the completion of treatment.

Approximately 55 % of the observation patients crossed over to receive Vidaza treatment, and of that crossover group, 12.8% demonstrated complete or partial response, the company said.

Vidaza is believed to exert its anticancer effects by causing demethylation, or hypomethylation, of DNA in abnormal blood-forming (hematopoietic) cells in the bone marrow as well as through its direct cytotoxic effect.

Demethylation may restore normal function to tumor- suppressor genes which are responsible for regulating cell differentiation and growth. The cytotoxic effects of azacitidine cause the death of rapidly- dividing cells, including cancer cells that are no longer responsive to normal growth control mechanisms. Non-proliferating cells are relatively insensitive to Vidaza.

The major toxicity was myelosuppression, as manifested by thrombocytopenia (and bleeding), neutropenia (and infections), and anemia, the agency said.

Myelosuppression decreased with the onset of a response. Other common adverse events were gastrointestinal (nausea, vomiting, diarrhea, constipation, anorexia), constitutional (fatigue, weakness, fever, rigors), musculoskeletal (arthralgia, pain in limb), pulmonary (cough, dyspnea), and skin and soft tissue (ecchymoses, rash, erythema).

"In addition to being the first drug approved for the treatment of MDS, Vidaza is the first of a new class of compounds called demethylation agents to be approved," Judith Hemberger, Pharmion co-founder and COO, said in a statement. "We look forward to further exploring the clinical role of Vidaza in the treatment of other cancers in which demethylation may provide a benefit."

"The approval of Vidaza represents a significant milestone for Pharmion and, more importantly, represents an important new option for patients being treated for Myelodysplastic Syndromes," Patrick Mahaffy, Pharmion president and CEO said in a statement. "Until today, there have been no approved therapies for the treatment of MDS. We are proud to have advanced the work of the NCI, the Cancer and Leukemia Group B, and other academic institutions and clinicians to the point that this drug can now be commercially available to treat this very serious and life- threatening disease."

"The CALGB is proud to have conducted the pivotal clinical trials involved in the development of Vidaza," said Richard Schilsky, associate dean for clinical research at the University of Chicago, and chairman of the CALGB. "We are delighted to have had the opportunity to work with Pharmion and to now see Vidaza move from an experimental therapy to an approved product. Most importantly, we believe the approval of Vidaza is an important step forward for patients with MDS."

Vidaza has been granted orphan product designation by the FDA that entitles the drug to seven years of market exclusivity for MDS in the U.S.

In September 2003, Pharmion initiated an additional

phase III/IV clinical trial comparing the effect of Vidaza to conventional care options on survival in patients with high-risk MDS. The study, which will examine survival outcomes as well as secondary endpoints, will recruit more than 350 patients at treatment centers across Europe, Australia and the U.S., and is one of the largest studies to date in this disease.

Prescribing information is available at http://www.fda.gov/cder/foi/label/2004/050794lbl.pdf

Taxotere Approval

The Taxotere approval was based on TAX327, a phase III multi-center global clinical trial designed to evaluate chemotherapy with Taxotere and prednisone in the treatment of men with metastatic, hormone-refractory prostate cancer.

Altogether, 1,006 six patients were randomized to one of three treatment arms: (1) mitoxantrone + prednisone (MTX + P), (2) weekly Taxotere (TXT qw) + prednisone, or (3) Taxotere once every three weeks (TXT q3w) + prednisone.

The trial met its primary endpoint of increasing survival.

The treatment arm of TXT q3w + prednisone demonstrated a statistically significant survival advantage over MTX+P control (median survival 18.9 vs. 16.5 months, respectively, p = 0.0094). The TXT qw + prednisone arm did not demonstrate an advantage in overall survival over the control arm.

Adverse events included anemia, neutropenia, infection, nausea, vomiting, anorexia, and fatigue. Adverse events occurring more frequently with TXT q3w compared to MTX+P included allergic reactions, fluid retention, sensory neuropathy, alopecia, nail changes, diarrhea, and stomatitis.

The approved dose for this indication is 75 mg/m2 docetaxel given intravenously as a 1-hour infusion every 21 days on day 1 plus 5 mg oral prednisone twice daily for 10 cycles.

The findings of the study supporting the approval will be presented June 7 at the plenary session of the annual meeting of the American Society of Clinical Oncology in New Orleans.

"This latest approval for Taxotere provides evidence that our drug can positively impact the lives of men around the world with this disease," Frank Douglas, a member of the board of management at Aventis said in a statement. "In addition, this FDA action makes Taxotere the only drug approved for breast, lung and prostate cancer, three of the most prevalent cancers in the world toda."

A regulatory submission for Taxotere in prostate cancer is also pending with the European Agency for the Evaluation of Medicinal Products, the company said.

Current therapy for advanced prostate cancer is hormonal manipulation. However, the effects of this treatment typically last between 24 and 36 months, at which time patients may become refractory to hormonal therapy and be considered candidates for chemotherapy, such as Taxotere.

Prescribing information is posted at http://www.fda.gov/cder/foi/label/2004/020449s028lbl.pdf

Gemzar Approval

The Gemzar approval was based on a multi-center, multinational, randomized trial in 529 patients comparing the combination of Gemzar and paclitaxel with paclitaxel alone.

The primary endpoint of the study was overall survival. Time to documented progressive disease was a co-primary endpoint. The drug was approved based on an interim analysis that demonstrated an improvement in time to documented disease progression.

Gemzar 1,250 mg/m2 (intravenous infusion over 30 minutes) was administered on Days 1 and 8 of a 21-day cycle with paclitaxel 175 mg/m2 (intravenous infusion over 3 hours) administered prior to Gemzar on Day 1 of each cycle. Single-agent paclitaxel 175 mg/m2 (intravenous infusion over 3 hours) was administered on Day 1 of each 21-day cycle as the control arm.

Gemzar in combination with paclitaxel resulted in statistically significant improvement in time to documented disease progression (median TtDPD 5.2 months versus 2.9 months, $p<0.0001$), and overall response rate (RR 40.6% versus 22.1%, $p<0.0001$) compared to monotherapy with paclitaxel.

The combination of Gemzar plus paclitaxel also showed a strong trend toward improved survival in an interim survival analysis.

The principal Grade 3 and 4 adverse effects of the Gemzar plus paclitaxel regimen were hematologic (neutropenia, anemia and thrombocytopenia). Grade 3 and 4 liver enzyme elevation was also more common with Gemzar plus paclitaxel treatment. Grade 3 and 4 non-laboratory toxicities associated with Gemzar plus paclitaxel therapy included fatigue, neuropathy and myalgias.

This is the drug's third indication in the U.S. The official label on the approval states that Gemzar, in combination with paclitaxel, is approved for the first-line treatment of metastatic breast cancer after failure of prior anthracycline containing adjuvant chemotherapy, unless

anthracyclines were clinically contraindicated.

The results will be presented at the annual meeting of the American Society of Clinical Oncology, June 5-8, in New Orleans.

"The Gemzar/Taxol combination is one of the few combinations to surpass the single-agent efficacy of Taxol," said Paolo Paoletti, vice president of oncology clinical research at Eli Lill. "In a disease that is marked by high recurrence rates, this added benefit is welcome news to patients and physicians."

Full prescribing information is available at http://www.fda.gov/cder/foi/label/2004/020509s029lbl.pdf

Capitol Hill:

Groups Call NCI Funding For Trials "Chump Change"

By Kirsten Boyd Goldberg

Accrual of cancer patients to clinical trials would increase if NCI provided more funding to the cooperative groups, a group chairman told a Congressional panel earlier this month.

NCI's $4.6 billion budget in fiscal 2003 provided $115 million to support the cooperative groups that develop and conduct clinical trials in adult cancers, said Robert Comis, chairman of the Eastern Cooperative Oncology Group and president and chairman of the Coalition of National Cancer Cooperative Groups. Peer reviewers recommended that the groups receive twice that amount, he said.

"$115 million out of a $4.6 billion budget is chump change," Comis said at a May 13 hearing of the House Committee on Government Reform. "NCI has to recognize that it needs to fund these groups."

Nationally, only about 3 percent of eligible adult cancer patients enroll in clinical trials, and only 15 percent of patients are aware that trials are an option. Trials would close faster and report results sooner if more patients enrolled, Comis said.

The cooperative groups enroll about 26,000 a year, about half of the estimated total number of cancer patients enrolled in trials each year. "The system is stressed even at this level of accrual," Comis said. "The cooperative groups have been and remain chronically under-funded. Two extensive reviews of the system in the mid-1990s recommended that the cooperative groups be funded at the full peer review recommended level. We continue to be funded at 60 percent of that level, and funding has been flat for the last three years."

NCI's lack of commitment to the groups "stifles innovation, cripples critical infrastructure like the tissue banks, data management, and informatics, and serves as a disincentive to academic and community physician participation," Rep. Henry Waxman (D-Calif.) said at the hearing.

"The federal government must adequately support a clinical research infrastructure that proves cures work," Waxman said.

NCI cut its funding for the adult cancer cooperative groups by nearly $6.3 million from fiscal 2002 to 2003, according to a chart Waxman displayed.

At the hearing, Committee Chairman Tom Davis (R-Va.) avoided criticism of the Bush Administration's budget. He called for more education for patients and physicians about clinical trials, better access to trials for patients in rural areas, and easing of eligibility criteria.

"Clinical trials are essential for improving outcomes in cancer patients," Davis said. "By improving participation levels and creating more trials to test new therapies, we can transform cancer into a more treatable and less fatal disease."

Michaele Christian, director of the NCI Cancer Therapy Evaluation Program, testified that funding for the groups increased more than 60 percent between FY98 and FY03, and support to cover patient enrollment "more than doubled from less than $1,000 at most sites to $2,000 at all sites."

NCI's per-patient reimbursement is only about half to a quarter of what it actually costs physicians and medical centers to enroll patients on clinical trials, Comis said. A survey by the American Society of Clinical Oncology found that the actual cost is about $4,000 to $6,000 per patient. Industry-sponsored trials generally reimburse physicians $5,000 per patient, and often provide support for data managers and specially trained nurses.

"The ability for both academic and community sites to continue to do government-sponsored work will be increasingly challenged, particularly when the full effect of the Medical Modernization Act of 2003 takes place in 2005," Comis said.

Under the MMA, total payments for cancer care are expected to drop precipitously in 2005, causing physicians to cut services such as clinical trial participation, said Ellen Stovall, president and CEO of the National Coalition for Cancer Survivorship.

The Congressional Budget Office estimated that drug payments will drop by $300 million in 2005, and payment for services will fall by more than 20 percent.

"For most oncologists, clinical research is a cost,

not a profit, center," Stovall said. "It seems inevitable that payment reductions of this magnitude will make it extremely difficult for oncologists in private office-based practice to continue the investment necessary to enable them to offer clinical trials as an option for their cancer patients."

Andrew Pecora, chairman and director of The Cancer Center at Hackensack University Medical Center and clinical professor of medicine at the University of Medicine and Dentistry of New Jersey, said slow accrual to trials stagnates the development process.

"It is not the lack of good ideas that is slowing progress in our quest to cure cancer, but it is much more a result of the slow pace of completing active clinical trials," Pecora said. He called for additional funding for hospital and office-based programs to support infrastructure that would allow more physicians and patients to participate in trials.

Richard Pazdur, director of the FDA Division of Oncology Drug Products, said the medical product development path has become challenging, inefficient, and costly. The agency's "Critical Path" report, released last March, details this problem. The report is available at www.fda.gov/oc/initiatives/criticalpath/.

"The problem, in FDA's view, is that the applied sciences needed for medical product development have not kept pace with the tremendous advances in basic sciences," Pazdur testified. "The new science is not being used to guide the technology development process in the same say that it is accelerating the technology discovery process.

"For medical technology, performance is measured in terms of product safety and effectiveness," he said. "Not enough applied scientific work has been done to create new tools to get fundamentally better answers about how the safety and effectiveness of new products can be demonstrated, in faster time frames, with more certainty, and lower costs.

"In many cases, developers have no choice but to use the tools and concepts of the last century to assess this century's treatment candidates," Pazdur said. "As a result, the vast majority of investigational products that enter clinical trials fail."

FDA is planning an initiative to identify and prioritize the developmental problems and opportunities for rapid improvement and public health benefits, Pazdur said. "Through scientific research focused on these challenges, we can improve the process for getting new and better treatments to patients," he said.

The hearing testimony is available at http://reform.house.gov.

Funding Opportunities:

Charles Culpeper Scholarships In Medical Science Offered

Application Deadline: Aug. 16,2004

Goldman Philanthropic Partnerships is accepting applications for its 2005 Charles E. Culpeper Scholarships in Medical Science Program to support the career development of academic physicians.

Up to three awards of $100,000 per year for three years will be made to U.S. medical schools or equivalent U.S. educational institutions on behalf of candidates who are U.S. citizens or aliens who have been granted permanent U.S. residence; who have received their M.D. degree form a U.S. medical school or the equivalent of an M.D. degree from an educational institution equivalent to a U.S. medical school in 1996 or later (except under extraordinary circumstances, as approved by Goldman Philanthropic Partnerships before submittal).

All scientific research relevant to human health is eligible for consideration; research that has relevance to cures for human disease is highly encouraged. No institution may nominate more than one candidate.

For application forms, see www.goldmanpartnerships.org. or contact Kenlyn Vass, Goldman Philanthropic Partnerships, 155 N. Pfingsten Rd. Suite 109, Deerfield, IL, 60015, phone 847-948-5512; fax 847-948-5516.

RFAs Available

RFA-HL-04-034: Cellular and Genetic Discovery Toward Curative Therapy in Myeloproliferative Disorders

Applications focused on the genetic and cellular characteristics associated with MPD are responsive to this RFA. Examples include but are not limited to: 1) mechanisms of action of hydroxyurea in ameliorating disease progression in MPD, 2) correlation of molecular profiles with chromosomal and gene specific alterations or mutations associated with MPD, 3) cellular and molecular profiles and other approaches for classifying the diagnosis, prognosis and disease progression of MPD, 4) cytometric characterization of premalignant clones and subpopulations in MPD, 5) demonstration of molecular markers that are associated with malignant transformation in MPD, and 6) stem cell biologic and animal disease models specific for MPD in order to explore etiologic hypotheses and therapeutic interventions. The RFA will use the NIH R01 award. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-HL-04-034.html.

Inquiries: For NCI--Allan Mufson, Division of Cancer Biology, phone 301-496-7815; e-mail am214t@nih.gov.

RFA-CA-05-013: Reducing Barriers to Symptom Management and Palliative Care

This RFA is soliciting grant applications for research

to develop and test interventions to overcome barriers to the delivery of symptom management and palliative care, thereby decreasing the suffering and improving the health and quality of life of persons living with cancer. Program staff at the NCI and other NIH Institutes and Centers that are participating in this RFA conceptualize symptom management as one component of the care delivered to cancer patients at risk for or experiencing disease-and treatment-related symptoms. Other components, as defined by the World Health Organization, include communication, decision-making, management of complications of treatment, psychosocial care of patient and family, and care of the dying. To address the complex and interdependent physical, social, psychological, and existential needs of patients and their families requires a multidisciplinary team approach.

The focus of this initiative is broad and includes cancer patients across the disease trajectory. Settings where interventions could be tested include, but are not limited to, acute care facilities, the home, skilled nursing facilities, outpatient clinics, and hospices. Given the significant number of cancer patients being treated in community settings, we are particularly interested in applications that would access this type of setting or would develop interventions that are generalizable to the broader community setting. for example, the unique research infrastructures of the Community Clinical Oncology Program and the HMO Cancer Research Network make them suitable for implementing these types of interventional research projects. The RFA, which is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-05-013.html, will use the NIH R01 research project grant and the R21 exploratory/developmental grant award mechanisms.

Inquiries: For NCI--Ann O'Mara, program director, Community Oncology and Prevention Trials Research Group, NCI Division of Cancer Prevention, phone 301-496-8541; e-mail omaraa@mail.nih.gov.

In Brief:

Einhorn, Young, Levin, Look, Foti, Kim Win ASCO Awards

(Continued from page 1)

been responsible for dramatically improved treatment response rates. About 90% of patients diagnosed with the disease make full recoveries. Einhorn is also credited with developing cisplatin, one of the most widely used chemotherapeutic agents, and he is recognized as an authority on other types of urologic cancer as well as lung cancer. He was elected to the National Academy of Sciences in 2001, served as ASCO president from 2000-2001, and is a member of the ASCO Foundation board. He received the Karnofsky award in 1990.

Robert Young, president of Fox Chase Cancer Center, will receive ASCO's Distinguished Service Award for Scientific Leadership, established to recognize the achievements of individuals who, through a blend of outstanding leadership skills and groundbreaking scientific vision, have transformed the practice and profession of medicine. The award recognizes Young's nearly 40 years of service in the field of oncology and his contributions to advancing the understanding of ovarian cancer. His groundbreaking studies determined the optimal procedures for staging early and advanced ovarian cancers, as well as the optimum treatment regimens. He developed the chemotherapy regimen of paclitaxel plus carboplatin, the standard of care for patients with advanced ovarian cancer. Young has also served as president of ASCO and the American Cancer Society. Young was chief of the NCI Medicine Branch for 14 years, where he was part of a team that developed combination chemotherapy regimens for Hodgkin lymphoma and diffuse large cell lymphomas.

Bernard Levin, vice president for cancer prevention at M.D. Anderson Cancer Center, will receive the American Cancer Society Award recognizing significant contributions to cancer prevention and control. Under his leadership since 1994, M.D. Anderson's Division of Cancer Prevention has grown into one of the largest and most comprehensive programs of its kind, designing prevention initiatives through interdisciplinary research in molecular epidemiology, chemoprevention, genetics, and behavioral science. He has made significant contributions to the identification of biochemical and genetic predeterminants for gastrointestinal cancers and has also been instrumental in the development of new treatment methods for these cancers. Levin's efforts to educate policy makers and the public have included testimony before Congress on behalf of the American Gastroenterological Association and have helped to procure Medicare coverage for colorectal cancer screening. He serves as chairman of ASCO's Cancer Prevention Committee, the ACS National Advisory Task Force on Colorectal Cancer, and the National Colorectal Cancer Roundtable.

A. Thomas Look, vice-chairman for research in pediatric oncology at Dana-Farber Cancer Institute, and professor of pediatrics at Harvard Medical School, will receive ASCO's Pediatric Oncology Lectureship, honoring individuals who have contributed outstanding scientific work in pediatric oncology. His major research interests are transcriptional control of programmed cell death in human acute leukemia and genetic abnormalities of childhood leukemia and solid tumors. Look's laboratory recently generated a model of T-cell acute leukemia in zebrafish that could prove significant in determining how other genes cooperate

with or antagonize the development of leukemia. Prior to his work at Dana-Farber, Look served as chairman of experimental oncology at St. Jude Children's Research Hospital. In recognition of his significant contribution to the field of pediatric leukemia, he received the Award for Excellence in Pediatrics by the American Society of Pediatrics and was recently named the Daniel Burton Endowment Fund Lecturer in Leukemia at the Hospital for Sick Children in Toronto.

Margaret Foti, CEO of the American Association for Cancer Research, will receive ASCO's Special Recognition Award for her instrumental role in the development of the ASCO/AACR Joint Workshop, Methods in Clinical Cancer Research, which has served as the prototype for subsequent workshops designed to introduce beginning oncologists in Europe and Australia to the essentials of effective clinical trials design. Foti began working for AACR in 1965 as an editorial assistant for the journal Cancer Research, and has served as CEO for the last 22 years.

Paula Kim, co-founder and president of the Pancreatic Cancer Action Network, will receive ASCO's Partners in Progress Award in recognition of her commitment to improving the quality of care for patients with pancreatic cancer. Established in 2003, this award honors extraordinary patient advocates whose dedication and work have had a measurable effect on public awareness about cancer and have led to advancements in cancer treatment, research, prevention, and education. Kim began her quest to inform and advocate on behalf of patients with pancreatic cancer and their families after her father was diagnosed with the disease in 1997.

Reps. Lois Capps (D-Calif.) and **Charlie Norwood** (R-Ga.) will receive ASCO's Public Service Award for their work to promote legislative solutions to preserve high-quality cancer care, including the introduction of H.R. 1622, the Quality Cancer Care Preservation Act, to reform Medicare payment for chemotherapy delivery. Capps serves as co-chairwoman of the bipartisan House Cancer Caucus. Norwood voted against the Medicare prescription drug bill in part due to the legislation's reductions to the cancer care delivery system.

ASCO will present Special Appreciation Awards to the following founders and founding directors in recognition of the society's 40th year: **Fred Ansfield, Harry Bisel, Michael Brennan, Joseph Burchenal, Herman Freckman, Emil Frei III, Arnoldus Goudsmit, Robert Talley, William Wilson, and Jane Wright**.

THE CANCER LETTER

Vol. 19 No. 5
May 2004

Business & Regulatory Report

Product Approvals & Applications:

Vidaza NDA For Myelodysplastic Syndromes Approved; FDA OK's 2 Supplemental NDAs

FDA approved one new application for a cancer drug and two additional uses for previously approved oncology drugs.

The agency approved an NDA for Vidaza (azacitidine for injectable suspension) for all subtypes of myelodysplastic syndromes. The full approval was based on response rates supported by reduction or elimination of transfusion dependence. The agent is sponsored by **Pharmion Corp.** (Nasdaq: PHRM) of Boulder, Colo.

The two supplemental NDAs are:

—Taxotere (docetaxel for injection) for use in combination with prednisone for the treatment of metastatic, androgen-independent (hormone

(Continued to page 2)

Clinical Trials:

Roche, Antisoma, Say Phase III Trial Of Monoclonal Didn't Meet Endpoint

Roche of Basel, Switzerland, and **Antisoma** of London said their SMART (Study of Monoclonal Antibody RadioimmunoTherapy) trial, a phase III study of R1549 in ovarian cancer, does not meet its primary endpoint.

The outcomes for R1549-treatment appeared no better than the outcomes for the comparative arm of the trial, the companies said. Given the findings, it is unlikely that development of R1549 will continue.

"The outcome of this study will have no impact on our growth outlook and we remain committed to our long-term relationship with Antisoma, which is based upon multiple products," said William Burns, head, Roche Pharmaceuticals Division.

Roche also said phase III data on Tarceva in non-small cell lung cancer will be the next regulatory submission for cancer. That would give the Roche group five cancer medicines with a proven survival benefit: Herceptin, MabThera, Xeloda, Avastin, and Tarceva, the companies said.

The SMART study is a phase III randomized, single-blinded parallel group trial that began in 1998, the companies said. The trial of more than 420 women with ovarian cancer in seventeen countries compared standard care plus R1549 to standard care alone. Women receiving R1549 were given a single dose of the drug via a catheter into the abdomen (intraperitoneal administration) after surgery and chemotherapy.

R1549 is a monoclonal antibody linked to the radioactive isotope

(Continued to page 3)

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

FDA Approves Two sNDAs: Taxotere And Gemzar

(Continued from page 1)

refractory) prostate cancer. The agent is sponsored by **Aventis Pharmaceuticals Inc.** (NYSE: AVE) of Strasbourg, France.

—Gemzar (gemcitabine HCl) in combination with paclitaxel for the first-line treatment of patients with metastatic breast cancer after failure of prior anthracycline containing adjuvant chemotherapy, unless anthracyclines were clinically contraindicated. The agent is sponsored by **Eli Lilly and Co.** (NYSE: LLY) of Indianapolis.

A story about the approvals appears in the May 28 issue of **The Cancer Letter**.

* * *

Ash Stevens Inc. of Detroit received approval from FDA to manufacture the Bulk Drug Substance 5-Azacitidine for Pharmion's Vidaza a treatment for Myelodysplastic Syndromes.

The FDA approved Vidaza for treatment of all five MDS subtypes. This is the first approved product to manage this life threatening condition.

5-Azacitidine will be manufactured in ASI's recently renovated Riverview, Mich., manufacturing facility beginning immediately. The 30,000 square foot state-of-the-art facility includes reaction vessels with capacities up to 500 gallons and a variety of product isolator systems including a Walker-Carlisle containment isolator for high potency drug substances.

* * *

Enzon Pharmaceuticals Inc. (Nasdaq: ENZN) and **Inex Pharmaceuticals Corp.** (TSX: IEX) said their NDA for Onco TCS (vincristine sulfate liposomes injection) has been accepted by the FDA.

The NDA is seeking marketing approval for Onco TCS as a single-agent treatment for patients with relapsed aggressive non-Hodgkin's lymphoma previously treated with at least two combination chemotherapy regimens.

Onco TCS is also being evaluated in several phase II oncology clinical trials, including first-line non-Hodgkin's lymphoma. Based upon its successes to date, we believe that Onco TCS has significant revenue potential, the company said.

In the completed multi-center pivotal phase II/III clinical trial for Onco TCS, 119 patients with aggressive NHL were treated who had not responded to their previous therapy or had responded and subsequently relapsed. After treatment, an overall response rate of 25% was attained. Currently, there is no standard treatment for patients with aggressive NHL that have relapsed following at least two prior treatment regimens.

The results of this pivotal trial were released in June 2003 and presented in December 2003 at the American Society of Hematology annual conference along with interim results from two ongoing phase II trials in relapsed Hodgkin's disease and relapsed B-cell lymphoma.

Onco TCS is comprised of the widely used off-patent anticancer drug vincristine encapsulated in INEX's liposomal drug delivery technology. INEX's technology is designed to provide prolonged blood circulation, tumor accumulation and extended drug release at the cancer site. These characteristics are intended to increase the effectiveness and reduce the side effects of the encapsulated drug.

Onco TCS is currently being evaluated in several phase II clinical trials as a treatment for first-line NHL, relapsed small cell lung cancer, relapsed Hodgkin's disease, relapsed acute lymphoblastic leukemia, relapsed pediatric malignancies, relapsed NHL in combination with the approved cancer drug Rituxan (rituximab), and relapsed NHL in combination with the approved cancer drug etoposide.

In January, Enzon and INEX announced a strategic partnership to develop and commercialize Onco TCS. INEX is a Canadian biopharmaceutical

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

Business & Regulatory Report is a supplement to The Cancer Letter and available separately for $155 per year. ISSN 1053-9611.

company developing and commercializing proprietary drugs and drug delivery systems to improve the treatment of cancer.

* * *

GlobeImmune Inc. of Aurora, Colo., said its Investigational New Drug application for the GI-4000 product series has become effective after the initial 30-day review, clearing the way for the company to initiate a phase I trial of the GI-4000 products.

The GI-4000 series is a new class of targeted immunotherapy products being developed for the treatment of a number of cancers, the company said. The series was developed using the company's yeast-based immunotherapy platform and targets a protein known as Ras that is mutated in a number of different types of tumors.

The GI-4000 series consists of three products (GI-4014, GI-4015, and GI-4016) directed to five specific mutations in the Ras protein.

The phase I trial is a multi-center, open label, dose escalation study designed to evaluate the safety, immunogenicity, and clinical benefit of the GI-4000 series in patients with tumors expressing Ras mutations. The study, to be conducted at approximately four sites in the U.S., will enroll 15 to 25 patients with stage III or IV colorectal, pancreatic, or non-small cell lung cancers, the company said.

* * *

Varian Medical Systems Inc. (NYSE:VAR) of Palo Alto, Calif., said it has received 510(k) clearance from FDA for a single-channel device for delivering High-Dose Rate brachytherapy.

The MammoSource afterloader is a computer-controlled device that delivers a high-energy radioactive source through a single catheter, into the cavity left when a tumor has been surgically removed, the company said. It works with the Varian BrachyVision software, an image guided HDR brachytherapy treatment planning system.

* * *

Viatronix of Stony Brook, N.Y., said its V3D-Colon system received FDA approval for the detection of colon cancer.

Results of a colonoscopy study found the system to be more reliable and accurate than other virtual colonoscopy systems, the company said.

"After performing a direct comparison of three different virtual colonoscopy systems, the only one system, the Viatronix system, was capable of a primary time efficient 3D reading, which is necessary for sensitive detection of polyps," said Perry Pickhardt, staff radiologist for the National Naval Medical Center, assistant professor of radiology for the Uniformed Services University of the Health Sciences, and associate professor of radiology at the University of Wisconsin Medical School. "For Polyps 8mm and greater, V3D-Colon outperformed optical colonoscopy, long considered the gold standard of colorectal cancer screening as reported in the clinical study published in NEJM."

The non-invasiveness of the V3D procedure eliminates the physical discomfort of a conventional optical colonoscopy, and the risk of perforation of the colon walls, the company said. The virtual colonoscopy requires no sedation, and normal activities can resume immediately after the 15-minute procedure.

* * *

Wilex AG, of Munich, Germany, said it has received FDA IND approval for a phase III trial of the antibody Rencarex (WX-G250) for renal cell carcinoma.

Wilex said it would evaluate the antibody versus placebo as an adjuvant therapy for non-metastasized RCC with high risk of recurrence after resection of the primary tumor. The company said it has discussed the study design with the European Agency for the Evaluation of Medicinal Products.

"This will enable us to start our multi-center international trial in Europe and the U.S. at the same time," Paul Bevan, head of R&D and member of the executive board of Wilex. "There are no approved treatment options at this point."

Rencarex (WX-G250), an IgG1 antibody that binds to a cell surface antigen, the MN-antigen, is found on 95% of clear renal cell carcinoma cells but not on normal kidney tissue, the company said.

Clinical Trials:

Roche Says R1349 No Better Than Standard Therapy

(Continued from page 1)

yttrium-90 using a chelating agent CITC-DTPA, the companies said. The antibody component binds to a protein, MUC1, found on the surface of ovarian cancer cells. R1549 was originally developed at the Imperial Cancer Research Fund (now Cancer Research U.K.) of London. Antisoma licensed the drug from Imperial Cancer Research Technologies (now Cancer Research Technologies) in 1996.

* * *

Cytokinetics Inc. (Nasdaq: CYTK) of South San Francisco said **GlaxoSmithKline** (NYSE: GSK) has initiated a phase I trial of SB-743921, the second small molecule inhibitor of kinesin spindle protein, for solid tumors.

The collaboration was established in June 2001 to discover, develop and commercialize small molecule therapeutics for cancer and other diseases, the companies said.

The open-label, non-randomized, dose-finding trial is investigating the safety, tolerability, pharmacokinetic and pharmacodynamic profile of SB-743921 in advanced cancers, the companies said.

SB-743921 is structurally distinct from SB-715992, the Cytokinetic most advanced drug candidate under the strategic alliance with GSK, for which GSK recently initiated a broad phase II clinical trials program to evaluate its effectiveness in different types of cancer, the companies said.

Drug candidates SB-715992 and SB-743921 are structurally distinct small molecule compounds that modulate cell proliferation and promote cancer cell death by inhibiting KSP, the companies said. KSP is a mitotic kinesin essential for cell proliferation.

* * *

FeRx Inc. of San Diego said enrollment has been stopped in a global multi-center phase II/III trial utilizing its proprietary MagneTarg drug delivery system with MTC-Doxorubicin for primary liver cancer (hepatocellular carcinoma or HCC).

"From a recent interim analysis, we determined that the clinical endpoints of the trial could not be met with statistical significance with the product as currently manufactured and therefore, it was necessary to immediately stop the trial," said Jacqueline Johnson, president and CEO of FeRx Inc. "As a result, the company has discontinued its plans for a venture capital financing and has developed contingency plans which include seeking strategic alternatives or closing the facilities."

The multinational MAGNET trial, was designed to enroll 240 patients in North America, Europe and Asia, the company said. The primary objective was to detect a clinically and statistically significant increase in median survival time for MTC-DOX treatment relative to treatment with IV doxorubicin, the comparator arm, the company said.

* * *

Matritech (AMEX: MZT) of Newton, Mass., said **Sysmex Corp** has begun clinical testing of the Matritec NMP179 Protein for cervical cancer screening.

The approach combines the Sysmex flow cytometry technology, the Matritech patented NMP179 protein biomarker and other technologies incorporated by Sysmex for rapid, detailed cell-by-cell analysis for cervical cancer, the company said.

"The beginning of a large-scale clinical trial is further validation of the utility of NMP proteins to accurately diagnose life threatening cancers," said Stephen Chubb, chairman and CEO of Matritech. "We have been pleased with the success of our NMP-based bladder cancer diagnostic product line and we look forward to utilizing our NMP technology to diagnose other cancers including cervical, breast and prostate."

* * *

Millennium Pharmaceuticals Inc. (Nasdaq: MLNM) of Cambridge, Mass., said it has initiated a multicenter phase II trial of Velcade (bortezomib) for Injection in combination with rituximab for relapsed or refractory indolent (follicular and marginal zone) non-Hodgkin's lymphoma.

The randomized study will assess efficacy, overall safety and tolerability of the combination in two different dosing schedules, the company said. The treatment is also being investigated in a range of phase I and II solid and hematologic tumors.

Velcade, a proteasome inhibitor, is approved in the U.S. and Europe for relapsed and refractory multiple myeloma, the company said.

The will be conducted at ten sites in North America and will enroll up to 66 patients with relapsed or refractory indolent B-cell lymphoma, including either follicular lymphoma or marginal zone lymphoma, the company said. Patients will be randomized to two arms to evaluate optimal dosing schedules; one arm will received 1.3 mg/m2 of Velcade (bortezomib) for Injection twice weekly and the other arm will receive 1.6 mg/m2 of Velcade weekly, both in combination with four weekly doses of 375 mg/m2 of rituximab.

The company said it is evaluating Velcade in a multicenter phase II trial for relapsed or refractory mantle cell lymphoma where one or two prior lines of therapy have been administered. Additionally, Millennium & Johnson and Johnson Research & Development, LLC continue to investigate Velcade in both hematologic and solid tumors, the company said.

* * *

Xanthus Life Sciences of Cambridge, Mass., said it has initiated a phase I/II study of its lead

oncology drug candidate, Xanafide (amonafide) in metastatic prostate cancer.

The study aims to define and validate the safety of a phenotypically driven dosing regimen using a biologically predictive test for drug metabolism to determine an individual's dosing needs for Xanafide, the company said. The study aims to evaluate the efficacy of Xanafide as determined by various measures of PSA response and tumor response.

Mario Eisenberger, professor of oncology and urology at Johns Hopkins Medical Institutions, is principal investigator for the study.

The phase I/II trial is an open-label, multi-center study of Xanafide in approximately 40 subjects with hormone refractory metastatic prostate cancer who may have had zero or one prior course of chemotherapy. The patient's initial dose will be determined by their metabolic phenotype as determined by Xanthus' proprietary testing approach.

Intravenous infusions will be administered weekly three weeks out of four for approximately five months. The primary objective of the study is to determine the safety of Xanafide using the company's approach to individualized dose adjustment. Xanthus will also evaluate the efficacy of Xanafide in this patient population.

Xanthus is using its metabolic phenotyping predictor technology to enable individualized dosing of Xanafide intended to optimize therapeutic outcome. Xanthus' technology provides a direct measurement of metabolic enzyme activity under conditions that mimic drug exposure.

Deals & Collaborations:

Israeli Firm Settles Patent Suit With Bristol-Myers Squibb

Teva Pharmaceutical Industries Ltd. (Nasdaq: TEVA) of Jerusalem said it has reached a settlement of patent litigation between its subsidiary **Pharmachemie** and **Bristol-Myers Squibb Co**. (NYSE:BMY) for carboplatin injection, the generic version of Paraplatin.

Under the settlement, Teva has entered into a supply and distribution agreement with Bristol-Myers Squibb for carboplatin injection (50 mg, 150 mg, 450 mg) and carboplatin aqueous solution injection (50 mg/5 ml, 150 mg/15 ml, and 450 mg/45 ml), the company said. The agreement will permit Teva to begin distributing the BMS products for the U.S. market at the end of June 2004.

The settlement allows Teva to seek final approval of its own abbreviated new drug applications for carboplatin with FDA, the company said.

Bristol-Myers Squibb had US sales of $769 million for Paraplatin in 2003. Teva will market and sell the products in the U.S. through its acquired subsidiary Sicor Inc., the company said.

* * *

AngioGenex Inc. of New York and **BioCheck Inc**. of Foster City, Calif., said they entered into an agreement to develop cancer diagnostic and prognostic products based on the Id-gene platform technology licensed exclusively to AGx by the Albert Einstein College of Medicine and the Memorial Sloan Kettering Cancer Center.

A phase I SBIR grant will provide seed funding for the collaboration, the companies said.

In adults, the presence of Id proteins is associated with the formation of tumors, the companies said.

* * *

BTG (LSE: BGC) of West Conshohocken, Pa., and **Cougar Biotechnology** of Los Angeles said they signed a license agreement by which Cougar is granted worldwide exclusive rights to develop and commercialize abiraterone acetate, for advanced prostate cancer.

BTG will receive an upfront cash payment and will benefit from further development milestones and a royalty on sales, the companies said.

Abiraterone was synthesized at The Institute of Cancer Research in the U.K. as part of a BTG-funded program to discover a selective, orally active drug to inhibit the key enzyme in testosterone synthesis, 17a hydroxylase/C17,20-lyase, the companies said. Suppression of testosterone synthesis was subsequently demonstrated in prostate cancer.

* * *

Corixa Corp. (Nasdaq: CRXA) of Seattle said it signed a 12-year agreement with the **Australian Nuclear Science and Technology Organization** of Sydney, Australia, in which Corixa grants ANSTO exclusive rights to develop, market and sell Bexxar (Tositumomab and iodine I 131 Tositumomab) therapeutic regimen in certain countries within Australasia, including Australia, New Zealand, Singapore, India, Indonesia and China. Corixa also grants ANSTO co-exclusive rights to supply Bexxar to Japan, South Korea and Taiwan.

Under the agreement, ANSTO will pay Corixa an undisclosed upfront licensing fee and will pay

Corixa milestone payments upon regulatory approval, obtaining reimbursement codes in Australia, approval for a second indication, as well as additional payments based on sales volume, the companies said.

ANSTO will pay Corixa royalties on all Bexxar sales in the exclusive ANSTO territories. Corixa will supply the cold antibody (Tositumomab) to ANSTO and ANSTO will perform radiolabeling at its facility in Lucas Heights, New South Wales

Bexxar was developed by Corixa and is co-marketed in the U.S. by Corixa GlaxoSmithKline for patients with non-Hodgkin's lymphoma.

* * *

Genzyme Corp. (Nasdaq: GENZ) said it has completed the purchase of the **Impath Inc.** (IMPHQ.PK) Physician Services business unit and other assets for $215 million in cash.

The assets will become part of the Genzyme Genetics business, the company said.

The acquisition of the unit, gives Genzyme an array of oncology diagnostics in solid-tumor and blood-based cancers, a team of board-certified anatomic and clinical pathologists with experience in oncology testing, and laboratories in New York City, Phoenix and Los Angeles. Genzyme will maintain operations at these facilities, the company said.

Genzyme also said it acquires the Impath Analytical Services unit, which includes an FDA-approved laboratory that provides clinical trial testing services to biotechnology and pharmaceutical companies for new drug evaluation.

* * *

Geron Corp. (Nasdaq: GERN) of Menlo Park, Calif., and **American Type Culture Collection** of Manassas, Va., said they entered into an agreement where Geron has granted to ATCC a non-exclusive license to create and distribute cell lines immortalized with human telomerase reverse transcriptase, and the hTERT gene itself, to the research-use-only market.

Telomerase is an enzyme that maintains telomere length and allows cells to divide indefinitely while retaining normal function and phenotype, the company said. Telomerase-immortalized human cells provide stable, uniform cell populations for functional cell-based assays and long-term gene expression studies. The cell lines can undergo repeated rounds of genetic engineering and scale-up, enhancing their use in biological studies, cell-based drug screens, and drug toxicity testing, as well as cell and gene therapy applications, the company said.

The license to ATCC excludes therapeutic or diagnostic use of hTERT, use in human clinical research, and certain other uses that would compete or conflict with the Geron product development programs, the company said.

Under the agreement, Geron said it will receive a license fee payment in cash as well as royalties on future product sales. Other specific financial terms of the agreement were not disclosed.

Geron said it has also designated ATCC as ex-situ repository and distributor of Geron-created immortalized cell lines and hTERT plasmids to non-profit institutions worldwide.

* * *

GTC Biotherapeutics Inc. of Framingham, Mass., said it has entered into agreements with **Mayo Clinic** to begin preclinical development of an agonistic antibody to CD137 for solid tumors.

The work will be funded by NCI through a phase I grant under the Flexible System to Advance Innovative Research For Cancer Drug Discovery by Small Business of the Small Business Innovative Research program, or FLAIR-SBIR, the company said.

The antibody was identified and underwent earlier stage research at Mayo Clinic.

The agreements define a collaborative relationship with Mayo Clinic to support the GTC development program, the company said. GTC will produce and purify the CD137 antibody and Mayo Clinic will collaborate on the preclinical testing.

The collaboration between GTC and Mayo Clinic will provide GTC with rights to patents that may issue under the patent applications that cover the CD137 antibody, the company said. Under the agreement, GTC has two years to exercise an option for an exclusive license to the patents, with Mayo Clinic providing oversight of the preclinical evaluations. GTC will produce two forms of the antibody that will be tested for bioactivity in human tumor models, and will seek additional grants to develop clinical production and testing, if appropriate, based on the results of the preclinical evaluations, the company said.

CD137, also known as 4-1BB, is a member of the tumor necrosis factor/nerve growth factor family of receptors and is a surface glycoprotein found on certain cells of the immune system, the company said. The agonistic antibody binds to and stimulates CD137 resulting in the strengthening of the otherwise weak immune response to tumors.

* * *

Insmed Inc. (Nasdaq: INSM) of Richmond,

Va., said **Department of Defense** has granted $10 million for therapeutic individualization in breast cancer treatment in a translational research project.

The Insmed rhIGFBP-3 has been selected as one of the candidate therapies for study, the company said. The lead investigator for the trials with rhIGFBP-3 is Brian Leyland-Jones of McGill University, former head of Developmental Chemotherapy at NCI.

The consortium of physicians, called the Breast Cancer Center of Excellence, will use genomics, proteomics, and pharmacogenetics to predict individual response to therapeutic agents in advanced breast cancer, the company said. The desired outcome of the study will be to maximize patient benefit while minimizing the toxic side effects of standard therapies on the market today.

* * *

Institute for Systems Biology of Seattle and the **Pacific Northwest National Laboratory** have entered into a partnership to expand technical capabilities of each organization in systems biology.

The collaboration would build the infrastructure to solve complex biological problems faster, refine the technological and computational abilities to measure and predict complex cell behavior, and strengthen existing collaborative research and development projects in systems biology, the companies said.

Current collaborations include computational approaches to predicting protein structure, said H. Steven Wiley, chief scientist and director of the Biomolecular Systems Initiative at PNNL, a Department of Energy laboratory based in Richland, Wash.

An ISB computational model for protein-folding is being run on the PNNL supercomputer, which is the fifth fastest in the world, said Wiley.

PNNL manages the NIH Proteomics Research Resource Center.

ISB and PNNL will become more competitive for several large DOE projects expected to begin in the next decade, including facilities for protein-tagging and whole proteome analysis, said Wiley.

In a related development, IsoRay of Richland, Wash, said it has signed a manufacturing contract with Pacific Northwest National Laboratory and U.S. Department of Energy to manufacture the Celsium-131 seed for prostate cancer under the Commercial Work For Others provision of the federal government.

"During the contract period, which expires at the end of September 2005, the company expects to finalize plans for the construction of its own manufacturing facility," said Roger Girard, chairman and CEO of IsoRay.

* * *

One Cell Systems Inc. of Cambridge, Mass., said it has been awarded a $956,149 phase II Small Business Innovation Research grant from NCI to develop a fluorescence in situ hybridization assay for detecting levels of telomerase mRNA in cancer cells.

Detection of telomerase expression at the mRNA level using FISH will permit identification of previously undetectable tumor cells in both blood and tissues, the company said.

* * *

OriGene Technologies Inc. of Rockville, Md., said the Cancer Drug Discovery Laboratory of the **Translational Genomics Research Institute** has acquired its TrueClone Kinase Collection for high-throughput drug target discovery and development.

TGEN research includes analysis of human genes and their role in modulating cancer drug sensitivity and resistance, the company said. Applications at TGEN will utilize cDNA clones for high throughput biology studies, and screening for biological function in mammalian cell based assays.

The OriGene TrueClone Collection includes over 75 percent of the NM sequences in the NCBI RefSeq database and covers 65-80 percent of the predicted human cDNA repertoire, the company said. Each cDNA clone matches an annotated mRNA reference sequence from established public domains and is housed in non-proprietary expression vectors suitable for transfection and direct in vivo or in vitro expression. The comprehensive nature of the TrueClone Collection and the uniformity and expression-readiness of the cloning vector enables a systems biology approach to high-throughput screening and functional studies, the company said.

Translational Genomics Research Institute is a non-profit biomedical research institute.

* * *

Pivotal BioSciences Inc., of Los Angeles and **ProteomTech Inc**. of Emeryville, Calif., said they are collaborating on the development of PB1, the Pivotal mutant IL-2 cancer therapeutic for renal cancer and melanoma.

PB1 is a low toxicity analog of interleukin-2, the companies said. Animal studies have demonstrated the agent solves the problem of

vascular permeability associated with wild-type IL-2 toxicity. Pivotal acquired the exclusive rights to PB1 from the University of Southern California, where it was discovered by Alan Epstein, professor of pathology.

* * *

Royal Philips Electronics (NYSE: PHG) of Andover, Mass., said its medical systems division has entered into a long-term research agreement with the **University of Chicago Hospitals**.

The agreement brings an array of state-of-the-art imaging equipment to the hospitals, including six CT scanners, several magnetic resonance scanners, diagnostic X-ray systems, nuclear medicine equipment and patient monitoring systems, as well as medical information and image processing technology.

In exchange, Philips gains access to the hospitals' experience in computer-assisted detection and diagnosis. The hospitals will serve as a national Philips reference site. Installation of the new equipment has begun and will continue through 2005.

Philips will support research efforts at the University of Chicago Hospitals on computer-assisted diagnosis for CT, especially for projects involving lung cancer; breast cancer using mammography, MRI and ultrasound; and development and testing of many other applications.

The research collaboration with Philips is expected to begin later this year and span a wide range of topics from pre-clinical development to improved clinical diagnosis and oncology applications.

* * *

Starbridge Systems of Salt Lake City said the NCI Advanced Biomedical Computing Center of Frederick, Md., purchased its Starbridge Hypercomputer, the first high-end reconfigurable computer acquired for bioscience research.

Based on consultation with Jack Collins of NCI, Starbridge produced a parallel and scalable implementation of the Smith Waterman algorithm, which is used to compare sets of genetic data, on the Starbridge Hypercomputer, the company said. The implementation of the algorithm enables NCI to compare genetic data sets of any size quickly.

As part of the final acceptance criteria, Starbridge demonstrated a Smith Waterman comparison of the human X to Y chromosomes. The comparison, which requires months of computation time on a cluster, was completed in five days on the Hypercomputer, the company said.

Oncology Management:

NCCN Updates Colorectal Clinical Practice Guidelines

National Comprehensive Cancer Network of Jenkintown, Pa., has updated the NCCN Colorectal Clinical Practice Guidelines. The NCCN Colon, Rectal, and Anal Cancer panel added two approved agents for advanced colon and rectal cancer and modified recommendations for adjuvant therapy for node positive colon cancer.

For first line therapy of advanced colon and rectal cancer, where intensive chemotherapy can be tolerated, bevacizumab (Avastin, Genentech) in combination with 5-FU based regimens including those using oxaliplatin or irinotecan were recommended to its list of treatment options, the panel said.

For second line therapy of colon or rectal cancer where either irinotecan could not be tolerate or where disease had proven refractory to irinotecan, cetuximab (Erbitux, ImClone Systems Inc. and Bristol-Myers Squibb Co.) was added as treatment options, the panel said.

The 5-FU, leucovorin, and oxaliplatin (Eloxatin, Sanofi-Synthelabo Inc.) combination is now considered an appropriate option for adjuvant therapy for node positive colon or rectal cancer where the primary tumor has been resected, the panel said.

* * *

Fischer Imaging Corp. of Denver and **InSiteOne Inc**. of Wallingford, Conn., have entered into a sales, marketing and support agreement that expands archive options for Fischer digital mammography customers with the InSiteOne management system.

InSiteOne said it provides the InDex product line, HIPAA-compliant pay-as-you-go, price per study services that include online, nearline and disaster recovery/business continuance image storage and access. InDex allows hospitals and imaging centers to leverage digital imaging technologies while reducing capital costs for storage equipment, maintenance, and IT professionals.

* * *

Premier Inc. and **R2 Technology Inc** of Sunnyvale, Calif., have executed a sole-source group buy agreement. The agreement, in effect through July 30, 2004, extends Premier members preferred pricing on the R2 Technology ImageChecker platform of CAD products for mammography, the companies said.

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.

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