THE CANCER LETTER INTERACTIVE

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NCI, FDA, Correlogic To Begin Large Trial Of Protein Pattern Diagnostic System

The NCI-FDA Clinical Proteomics Program plans to begin a large-scale trial this fall of its protein pattern diagnostic system in development as a non-invasive blood test for ovarian cancer.

The trial will be designed to produce the data required by FDA to evaluate the system for a Premarket Approval Application for Class III medical device approval, Lance Liotta, co-director of the proteomics program, said this week.

In development over the past year, the computer-assisted test

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In Brief:

Ann Landers, Columnist Who Urged Support For National Cancer Act of 1971, Dead At 83

ANN LANDERS, the advice columnist and a former member of the National Cancer Advisory Board, died June 22 at age 83. Her real name was Esther Pauline Friedman Lederer. The Chicago Tribune, which syndicated her column since 1987, said she died at home of multiple myeloma. Her column was printed in 1,200 newspapers. In 1971, she asked readers to write to their members of Congress and urge them to support the National Cancer Act. The column generated more letters to Congress than it had received in its history. The legislation appropriated $100 million for cancer research. In 1985, she received the Albert Lasker Public Service Award for that effort. In 1980, President **Jimmy Carter** appointed Lederer to a six-year term on the NCAB. She also served on the Advisory Committee to the Director, NIH. Lederer was born in Sioux City, Iowa, and attended Morningside College. She began writing her column in 1955. . . . **CITY OF HOPE** National Medical Center has been awarded $200 million in punitive damages by a Los Angeles County Superior Court jury in its lawsuit against Genentech Inc. The jury determined that Genentech breached its fiduciary duty to City of Hope and acted with “malice” or “fraud” when concealing numerous licenses to technology based on research conducted by City of Hope scientists **Arthur Riggs** and **Keiichi Itakura**. Riggs and Itakura conducted their research under a 1976 agreement between City of Hope and Genentech. This research, which resulted in over 100 patents held by Genentech worldwide, led to the creation, among other things, of synthetic insulin, or Humulin. The punitive award follows an award of $300.1 million in compensatory damages announced on June 10. Genentech is expected to

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NCI Intramural Science:

NCI-FDA Program Hopes To Commercialize Cancer Test

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successfully differentiated benign from malignant ovarian cancer with sensitivity of 100% (95% confidence interval of 93-100), specificity of 100% (87-99), and positive predictive value of 94% (84-99).

The results were published in the Feb. 16 issue of The Lancet.

The test identified all 50 ovarian cancer cases in a masked set, including all 18 stage I cases. The test recognized 63 of 66 cases of non-malignant disease.

The current standard biomarker for ovarian cancer, CA125, is elevated in about 80% of women with advanced disease and only 50-60% of women with stage I disease. The positive predictive value of CA125 plus ultrasound screening is about 20%.

"At this point, we can't consider population screening, but for those patients with abnormalities, we want to study this new way to help clinicians decide whether to do a biopsy," Liotta said to the NCI Board of Scientific Advisors at its June 24 meeting.

If successful in the larger study, the new method—which requires only a drop of blood from a patient—would not only improve ovarian cancer diagnosis, but could also revolutionize the field of cancer diagnostics as the investigators develop the system for other types of cancer.

"This study represents potentially a tremedous advance for the diagnosis and detection of ovarian cancer," NCI Director Andrew von Eschenbach said.

"In this partnership, FDA will provide the guidelines needed for approval and validation of the study, and NCI will serve as the reference laboratory that will collect all of the samples from around the country. That will enable us to shepherd this study through to cut the conventional five-year time to marketing down to an expected two years."

The test builds on Liotta's invention of laser-capture microdissection, which enabled researchers for the first time to analyze purified populations of cells directly from patient tissue samples. These studies showed that the pattern of proteins present in tissues or blood can be used to identify and characterize types of cancer.

In the testing system, a blood sample is placed on a protein chip and analyzed on a Protein Biology System 2 SELDI-TOF mass spectrometer. The machine blasts the blood sample with a laser beam, causing the proteins to fly off and land at various points on the chip. The protein cluster is then examined by computerized "time-of-flight" analysis.

Using artificial intelligence software developed by Correlogic Systems Inc., of Bethesda, Md., the computer is trained to distinguish between patterns found in malignant versus benign disease.

"The output can give you a cancer/no cancer or no match answer," Liotta said. "We can say to the clinician, in 95% of patients in this trial, this pattern was an indication of cancer. Right now we can't discriminate by tumor types, but we could train the computer to do that."

The system becomes more accurate over time as data from more patients are compared to the historical record of previously analyzed patterns, Liotta said.

Liotta and proteomics co-director Emanuel Petricoin of the FDA presented updated data from their ovarian cancer study at the NCAB meeting. The method correctly identified stage I ovarian cancer in 36 of 36 samples and ovarian cancer stages II, III, and IV in 75 of 76 samples, for an overall sensitivity of 99%. The system correctly identified "no evidence of disease" in 66 of 67 patients and benign gynecologic (cysts, fibroids) and non-gynecologic inflammatory conditions in 70 of 71 patients, for a

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total specificity of 99%.

NCI also has a trial underway with patients in treatment for ovarian cancer to see if the new technology can detect early recurrence. Elise Kohn of NCI is the principal investigator.

In collaboration with David Ornstein of University of North Carolina at Chapel Hill, the researchers are studying the system for use in diagnosing prostate cancer, with the goal of achieving better results than the current standard PSA test.

In the study in preparation for FDA filing, the NCI Laboratory of Pathology will act as the reference laboratory and lead institution, Liotta said. Serum will be provided through cooperative groups and other extramural programs. Groups that have confirmed their participation include: Northwestern Ovarian Cancer Early Detection Program, Memorial Sloan-Kettering Cancer Center High Risk Screening Program; Pacific Ovarian Cancer Research Consortium, Rhode Island State Consortium, and the Gynecologic Oncology Group. Discussions with other groups are underway.

The system may qualify for expedited PMA review because it represents a "breakthrough" technology and offers significant advantages over existing approved alternatives, Liotta said.

At the BSA meeting, board member Robert Young, president of Fox Chase Cancer Center, suggested that the system might help reduce the overtreatment of women diagnosed with early ovarian cancer. Almost all of these patients get adjuvant therapy, but only a third of them need it, he said. There is no method to predict which cancers are at greater risk of progression.

"As long as we can get serum samples prior to chemotherapy treatment, we could back-correlate" the outcomes of the patients to their protein pattern, Liotta said. It might then be possible to train the computer to recognize the pattern of the more aggressive tumors.

Board member John Minna, director of the Hamon Center for Therapeutic Oncology Research at University of Texas Southwestern Medical Center, cautioned the scientists as they move the system through the approval process and to marketing that they will need to be able to "demonstrate to the public that this is not a sweetheart deal between the NCI and the FDA."

"Nobody knows better about the graveyard of bad biomarkers than the FDA," Petricoin said. "FDA is not providing any more access [to its review process] to us than to any company."

"We will be under higher scrutiny," Liotta said.

Correlogic, which designed the Proteome Quest software, has a research agreement and a Cooperative Research and Development Agreement with NCI and FDA. The arrangement provides for the commercialization of the intellectual property rights associated with the concept of patterns of molecular expression as a diagnostic tool. This will allow Correlogic to enter into sub-licensing, joint venture and other agreements with for-profit and non-profit organizations, the company said.

The three organizations jointly own the rights to "A Process for Discriminating between Biological States Based on Hidden Patterns from Biological Data," the patent application licensed from NIH that describes the methodology of discovering disease states through the analysis of patterns of protein expression.

Patterns Of Gene Expression Predict Response To Treatment

NCI intramural scientists and university collaborators reported in the June 19 New England Journal of Medicine that patterns of genes that are active in tumor cells can predict whether patients with diffuse large B-cell lymphoma are likely to be cured by chemotherapy.

Researchers analyzed thousands of genes in lymphoma biopsy samples from patients with DLBCL and determined that the activity of as few as 17 genes could be used to predict patients' response to treatment.

"We're able to reliably predict the survival of these patients using data from a small number of genes, indicating that this technique should be entirely manageable for routine use," said NCI investigator Louis Staudt, the senior author on the study.

Profiling gene expression in patients' tumors may help clinicians decide which patients are suitable candidates for standard therapy and which should consider other options for treatment.

The discovery of the predictive genes relied on DNA microarray technology, which allows researchers to determine which genes are active within cells. Microarrays, also known as gene chips, are glass slides that have been coated with thousands of spots of DNA, each representing a different gene. When a gene is active in a cell, it produces RNA copies known as transcripts. To measure the activity

of genes, researchers use the RNA transcripts to make a fluorescent gene probe. When these gene probes are allowed to bind to their corresponding DNA spot on the chip, those spots on the chip light up. Scientists use the pattern and intensity of light emitted to determine the activity of each of the chip's thousands of genes.

For this study, researchers used the Lymphochip, a specialized microarray containing more than 12,000 DNA spots representing genes expressed in normal and malignant lymphoid cells. Developed as part of the NCI's Cancer Genome Anatomy Project, the Lymphochip is particularly useful for finding differences in gene expression among lymphoid cancers.

Staudt and his colleagues profiled gene expression in 240 tumor biopsies from patients with DLBCL and identified more than 600 genes whose expression varied significantly between patients who had responded well to treatment and those whose response was poor. These genes highlight aspects of the tumors that affected response to therapy, including how fast tumor cells were dividing and from what type of normal lymphocyte the tumor originated. Many of the predictive genes suggest that a patient's immune response to the tumor is important for achieving a cure with chemotherapy.

Focusing on genes where the difference in expression was most dramatic between the two groups of patients, researchers narrowed the key genes down to 17. From these genes, the investigators created a formula that could be used to predict survival following chemotherapy. This predictor classified the patients into four groups of equal size. The five-year survival rates for these groups were 73 percent, 71 percent, 34 percent, and 15 percent.

Currently, physicians rely on the International Prognostic Index to evaluate patients with DLBCL. This predictive index is based on clinical factors including age, stage of the tumor, and the presence of disease that has spread outside the point of origin. While useful for some purposes, Staudt noted that the IPI has not been successful in identifying the best candidates for alternate therapies.

"Based on variations in gene expression, we can now do a better job of predicting patient outcomes," he said.

Staudt said 32 of the 240 patients in this study were classified in the group with the poorest prognosis according to the IPI. Of these, four were in fact cured by standard chemotherapy. Gene expression profiling successfully identified each of these.

For those that don't respond to chemotherapy, alternatives are available.

"For half of the patients with diffuse large B-cell lymphoma, conventional chemotherapy appears to be a reasonable option, but for patients in the poor-risk group, we have to consider other therapies," Staudt said. One possibility for some patients would be a bone marrow transplant. There are also numerous clinical trials for which these patients may be eligible.

One option is PS-341, a new agent that targets a pathway in the cell that blocks chemotherapy. Gene expression profiling revealed that in DLBCL patients who do not respond well to standard chemotherapy, lymphoma cells have activated this pathway, known as NF-kB.

Based on these results, a phase II clinical trial of PS-341 along with standard chemotherapeutic agents is planned to begin later this year at NCI and other institutions. Blocking the NF-kB signaling pathway with PS-341 will allow DLBCL tumor cells to die more readily, which researchers hope will improve patient survival.

This trial will enroll DLBCL patients who have relapsed after standard chemotherapy. Gene expression profiles of the patients' tumors will be determined prior to treatment to understand which patients respond best to this new regimen.

Trials designed to correlate clinical results with molecular data will allow researchers to identify drugs that are effective in subgroups of cancer patients, an approach that has already proven effective in finding new agents to treat breast cancer and leukemia. Staudt said gene profiling will make it possible to obtain more information from clinical trials in the future.

"It makes sense to get the maximum amount of information from patients' valuable participation in clinical trials," he said. "It's a better investment in the research for both doctors and patients."

This research was sponsored by NCI as part of the Lymphoma/Leukemia Molecular Profiling Project and the NCI Director's Challenge.

The participating institutions included the University of Nebraska Medical Center, Omaha; the British Columbia Cancer Agency, Vancouver; the Norwegian Radium Hospital, Oslo; the University of Wuerzburg, Germany; the University of Barcelona, Spain; the Southwest Oncology Group; and the NCI Center for Cancer Research.

Research Funding:

Keep Giving New PIs A Break, Grant Policy Advisors Tell NCI

NCI should continue its policy of giving new investigators a slightly better chance of winning grant funds, an advisory group said in a report to the Institute.

The National Cancer Advisory Board Ad Hoc Working Group on Research Project Grants listed the support of new cancer researchers as the first priority in a list of six "guiding principles" it said NCI should follow.

NCI Division of Extramural Activities Director Marvin Kalt presented the report to the NCAB on June 11 and the Board of Scientific Advisors on June 24.

The NCAB convened the group to help NCI develop spending guidelines as it confronts the possibility of tighter budgets in coming years.

The NCAB working group proposed the following "guiding principles" for the Institute:

1. NCI should continue to give special consideration to supporting new investigators.

2. NCI should identify and initiate special one-shot supplement initiatives in FY 2003.

3. NCI could implement a targeted and more restrictive cap on competing renewal (type 2) requests.

4. NCI should continue the Accelerated Executive Review process.

5. NCI should engage in a top-to-bottom review of budgets with the Institute in order to establish the relative value of different initiatives which are ongoing.

6. NCI should strongly oppose any proposed change in the modular grant ceiling.

NCI Director Andrew von Eschenbach said the Institute is developing budget scenarios to prepare for significantly tighter budgets. "We are doing everything we can to make sure the success rate doesn't fall below 20%," he said.

Von Eschenbach noted that the trend in research is toward greater collaboration. "Studies in the future may require larger amounts of funding," he said.

Groups Oppose OMB Plan

President Bush proposed a budget of $4.7 billion for NCI in fiscal year 2003 as part of the completion of doubling the NIH appropriation. However, the White House Office of Management and Budget said it plans to propose only a 2.2 percent increase for NIH and its institutes in FY2004 through 2007.

Nearly half of the NCI budget funds Research Project Grants, most of which are awarded on a multi-year basis. The budget increases of the past four years resulted in new multi-year grants. NIH officials have said that in the case of a sharp drop in funding, the priority will be to maintain non-competitive renewals (**The Cancer Letter**, June 14, Vol. 28 No. 24).

Professional societies have begun efforts to oppose the OMB funding plan. In the May 24 issue of Science magazine, officials of three organizations showed that the OMB plan would wipe out the gains made by the doubling effort by FY2007. The result would be "alarming" and would "create wrenching choices for NIH and the research community."

The article, "NIH in the 'Postdoubling' Era," by officials of the Association of American Medical Colleges, the Federation of American Societies for Experimental Biology, and the Association of American Universities, said that growth below 6 to 8% "will negate many of the advantages achieved by the doubling and will undo the benefits of this extraordinary and bold policy decision. They will also severely strain the relationship of trust between NIH and its awardees on which our nation's successes in biomedical research rest."

FY 2002 Financial Management Plan

For FY 2002, NCI established the following financial management plan for awarding grants:

—Limit programmatic reductions to 5 percent for competing R01 awards within the payline when the direct cost awarded is 7 modules ($175,000) or lower. Larger competing R01 grants will receive programmatic reductions of approximately 11 percent. Modular grants will be funded with no escalation factor for future years.

—In general, future year commitments for non-modular grants will be calculated by using the FY 2002 award level as a base and applying a 3 percent escalation factor for recurring costs. Appropriate adjustments will be made for non-recurring costs, such as equipment.

—New (type-1) P01 grants will sustain reductions of approximately 15 percent from levels recommended by peer review.

—Competing renewal (type 2) awards, whose requested level has been capped at 20 percent over the previous year funding, will be reduced 6 percent

from peer review recommendations. This includes Program Project Grants (P01s) for the full year and traditional research grants (R01s) from the third review round (submitted on the receipt date October/ November 2001).

The Institute also set aside:

—$8 million exception allocation for Accelerated Executive Review exception requests.

—$7 million exception allocation for first time R01 investigators which will effectively extend the payline for eligible applicants near the 24th percentile.

—$20 million exception allocation for high priority P01s and R01s outside the paylines.

Also, NCI will select R01s which are 100 percent devoted to pancreatic research for funding up to 50 percent beyond the standard R01 payline (up to the 33 percentile). Pancreatic applications in other mechanisms (such as R03s or R21s) will also be given special consideration.

Philanthropy:

American Cancer Society Funds $54 Million In Grants

The American Cancer Society said it has funded 154 research and training grants, totaling $54 million, to begin July 1. Of these grants, 39 were renewals and 115 were new awards.

The research awards include 35 postdoctoral fellowships, 59 research scholar grants for beginning investigators, four targeted research grants directed at poor and underserved populations, 15 institutional research grants, and 36 health professional training grants.

The three largest research scholar grants for beginning investigators were for $864,000 over a four-year period. These were awarded to Jin Chen, Vanderbilt University; William Murphy, University of Nevada; and Karen Smith-McCune, University of California, San Francisco.

Another of the research scholar grants being funded was for Gloria Borgstahl, a biochemist at the University of Toledo in Ohio, for her work in basic molecular processes with proteins that cause breast cancer. Recently, NASA's space shuttle Atlantis returned to Earth with the first biological crystals that she grew on the international space station.

Among the health professional training grants, four Cancer Control Career Development Awards for Primary Care Physicians were awarded, the largest number funded at one time, totaling nearly $660,000. These junior faculty members will pursue academic careers with an emphasis on cancer control.

Also, 86 applications, ranked excellent to outstanding by the peer review committees, were approved for funding if additional funds become available through cancellations of awarded grants or by special donations for research.

Funding Opportunities:

Cancer Prevention Award

Nomination Deadline: Aug. 1, 2002

American Association for Cancer Research and the Cancer Research Foundation of America invite applications for the AACR-CRFA Award for Excellence in Cancer Prevention Research for investigators in basic, translational, clinical, epidemiological, or behavioral science investigations in cancer prevention research.

The winner of the award will present a lecture during the first AACR Frontiers in Cancer Prevention Research Meeting, which will be held Oct. 14-18, 2002 in Boston. The awardee will receive an honorarium of US$5,000, a commemorative plaque, support for travel and expenses to attend the meeting.

The award is open to all cancer researchers who are affiliated with any research institution anywhere in the world. Candidates may not nominate themselves.

For further information, see http://www.aacr.org/1620.asp.

Landon-AACR Prizes

Nomination Deadline: Aug. 16, 2002

Kirk A. & Dorothy P. Landon Foundation and the American Association for Cancer Research are calling for nominations for the two 2003 Landon–AACR Prizes for translational cancer research. The recipient of each prize will receive an unrestricted cash award of $200,000. Recipients give a scientific presentation at the AACR Annual Meeting (April 5-9, 2003 in Toronto) and participate in a symposium at the Sylvester Comprehensive Cancer Center at University of Miami in early 2004.

—**Kirk A. Landon-AACR Prize for Basic Cancer Research** recognizes significant, fundamental contributions to laboratory research.

—**Dorothy P. Landon-AACR Prize for Translational Cancer Research** recognizes extraordinary achievement in translational cancer research—the interface between basic research and

its application to the clinic in the areas of diagnosis, treatment, or the prevention of cancer.

The prizes are open to all cancer researchers affiliated with any research institution (academic, industry, government, or other) anywhere in the world. Institutions or organizations are not eligible, and candidates may not nominate themselves. Candidates must maintain an active research program and have a record of recent publications. Candidates will be considered on the basis of the seminal quality, scientific novelty, innovation, and significance of their basic and translational cancer research and its contribution to the acceleration of progress against cancer and its implications for future discoveries and application to continued cancer research. Candidates also will be considered on the basis of their presentation skills. Nomination forms are available at: http://services.aacr.org/landon.asp.

Inquiries: American Association for Cancer Research, Landon-AACR Prize Selection Committees, Public Ledger Bldg., Suite 826, 150 S. Independence Mall West, Philadelphia, PA 19106-3483.

PanCAN-AACR Award

Application Deadline: Oct. 15, 2002

American Association for Cancer Research and the Pancreatic Cancer Action Network invite applications for the Career Development Award for early-career scientists engaged in pancreatic cancer research. The two-year grant provides $50,000 per year for direct research expenses and support for travel to the 2003 and 2004 AACR annual meetings.

Further information: http://www.aacr.org/1603.asp. Inquiries: Michelle Muething, director of Patient and Liaison Services and Scientific Affairs, Pancreatic Cancer Action Network, Inc., PO Box 1010, Torrance, CA 90505, phone 310-791-5214; fax 310-791-5224; Web site http://www.pancan.org.

NCI RFA Available

NCI Specialized Programs of Research Excellence (SPOREs) in Human Cancer for the Year 2003

The objective of the initiative is to further develop the SPORE through the introduction of new translational research programs focused on cancers of the skin, ovary, gastrointestinal tract, brain, head and neck, as well as leukemias and lymphomas. A SPORE conducts translational research that requires interdependence between basic and clinical investigators in both the planning and implementation of research and emphasizes the application of basic research findings to patients and populations.

A SPORE is awarded to an institution and a group of investigators that will make a strong commitment to the organization and conduct of the program. The SPORE must demonstrate a balanced approach to research on prevention, etiology, screening, diagnosis and treatment of human cancer that translates basic research findings into innovative interventions applied to patients and populations. A SPORE must foster interactions between laboratory and physician scientists; identify new research opportunities that may have an impact in reducing cancer incidence and mortality; encourage collaborations both within and outside of its institution(s) (including interactions with other SPOREs); provide career development opportunities for new, independent investigators who wish to pursue active research careers in translational cancer research; and develop human cancer tissue resources that will benefit translational research. The full description is available at http://deainfo.nci.nih.gov/concepts/TPA-02-139.htm.

Inquiries: Jorge Gomez, Organ Systems Branch, Office of Centers, Training, and Resources, ODDES, NCI, phone 301-496-8528; e-mail jg1w@nih.gov.

Pre-Application Meeting

The Behavioral Research Program of the NCI Division of Cancer Control & Population Sciences has scheduled a pre-application informational electronic meeting, July 1, 3:30-5:30 p.m., for investigators planning to submit applications in response to Request for Applications RFA- CA-03-007: Centers of Excellence in Cancer Communication Research.

Representatives from the several NCI offices will be available to answer questions. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/rfa-ca-03-007.html.

Participants may register with Dana Thigpen at thigpend@mail.nih.gov. Inquiries: K Viswanath, Health Communication and Informatics Research Branch, Behavioral Research Program, DCCPS, NCI, 6130 Executive Blvd, MSC 7363, EPN Rm 4070, Bethesda, MD 20892-7363 [Rockville, MD 20852 - express mail], phone 301-594-6644; fax 301-480-2087; e-mail vv27s@nih.gov

In Brief:

NCI Advisors Complete Terms; Louisville Opens Imaging Center

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appeal both judgments. City of Hope said the awards will not affect the license it granted to Genentech for use of its monoclonal antibody technology. This technology is used in the manufacture of Herceptin and Rituxan. . . . **NCI DIRECTOR Andrew von Eschenbach** thanked 11 members of the NCI Board of Scientific Advisors for completing their six-year terms at the board's meeting June 24. They were: **Suzanne Fletcher**, of Harvard Medical School; **Waun Ki Hong**, of M.D. Anderson Cancer Center; **Tyler Jacks**, of Massachusetts Institute of Technology; **Amy Langer**, National Alliance of Breast Cancer Organizations; **Caryn Lerman**, of University of Pennsylvania School of Medicine; **Franklyn Prendergast**, of Mayo Cancer Center; **Joseph Simone**, of Simone Consulting**; Louise Strong**, of M.D. Anderson; **Daniel Von Hoff**, of Arizona Cancer Center; **Barbara Weber**, of University of Pennsylvania Cancer Center, and **Alice Whittemore**, of Stanford University School of Medicine. . . . **UNIVERSITY OF LOUISVILLE** Health Science Center has dedicated the Molecular Imaging Research Center at the James Graham Brown Cancer Center. The three components of the MIRC are a PET/CT scanner, a cyclotron, and two nuclear magnetic resonance spectrometers. "The MIRC can focus on the prevention of cancer at the molecular level by designing drugs that will turn off cancer-causing genes," said **Donald Miller**, director of the cancer center. . . . **MULTIDISPLINARY CARE** of Head and Neck Cancer, an Internet-based textbook, was published by The University of Texas M. D. Anderson Cancer Center. Interdisciplinary in its approach, the Web book takes a comprehensive approach to cancers of the mouth, throat, larynx, nasal cavity and sinuses, jaw, thyroid, salivary gland, skull base, eye and skin of the head and neck region. It covers surgical treatments that restore form and function, rehabilitation of speech and swallowing, nutrition and pain management. Other treatment topics include chemotherapy, radiation therapy, oncologic dentistry and prosthodontics. The Web book is targeted to health care professionals and students. "Because of the medium we are using, the information on new techniques and research findings can be updated regularly and quickly, allowing the book to evolve continually," said **Helmuth Goepfert,** chairman of the Department of Head and Neck Surgery at M. D. Anderson and editor of the project. The book is available at *www.headneckcancer.org*. . . . **W.K. YUNG,** professor of neurology and the Florence M. Thomas Professor of Cancer Research at M. D. Anderson Cancer Center, has been named chairman of the Department of Neuro-Oncology in the Division of Cancer Medicine at the center. His research includes clinical trials with agents including temozolmide, thalidomide, and cis-retinoic acid for glioblastoma. He also is developing a molecular therapy program targeting the PTEN/PI3K, EGFR and VEGF pathway abnormalities present in malignant glioma. Yung is the principal investigator of the NCI-sponsored Brain Tumor Consortium, conducting phase I and phase II trials of gene therapy strategies as well as anti-angiogenesis agents such as SU5416, PTK787 and PKI166. . . . **MELISSA CHAPMAN** was named HHS chief information officer in the Office of the Assistant Secretary for Budget, Technology and Finance. Chapman will oversee information technology resources, program systems and infrastructure. She will also be responsible for the development of enterprise architecture in compliance with the Office of Management and Budget's regulations and administration policy. Chapman was chief information officer for FDA. . . **HHS SECRETARY TOMMY THOMPSON** on June 10 urged pharmaceutical companies to cut the cost of prescription drugs to avoid a consumer backlash that could result in price controls. In the keynote address to the Biotechnology Industry Organization convention in Toronto, Thompson said the "ire of consumers" may push lawmakers to set price limits on prescription drugs. "People are going to start questioning why drugs are so much more expensive in the United States than in Canada, Mexico and Europe. That is going to add to the regulatory fervor," he said. He added that while he was not proposing price controls, drug makers could "avoid such an outcome" by lowering prices. Thompson said the pharmaceutical industry also "should be pressing hard" for a Medicare prescription drug benefit. Thompson noted that the government is working with drug companies, particularly on easing research and development of new drugs. That process "devours cash," Thompson said, adding that companies also spend a considerable amount of money during the FDA approval process. Thompson said the FDA is working to shorten the review process.

THE CANCER LETTER

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Business & Regulatory Report

Deals & Collaborations:

FTC Seeks To Block Merger Of Diagnostics Companies Cytyc Corp. And Digene Corp.

Federal Trade Commission is seeking a preliminary injunction to block the **Cytyc Corp.** proposed $420 million acquisition of **Digene Corp**.

According to FTC, the combination of the companies would lead to reduced competition and increased consumer prices within the highly concentrated market for primary cervical cancer screening tests, both now and in the future.

"The merger as proposed raises serious competitive concerns within the highly concentrated market for this important diagnostic tool," said

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Product Approvals & Applications:

FDA Issues Non-Approvable Letter To AstraZeneca For sNDA For Casodex

AstraZeneca said FDA has issued a non-approvable letter for its supplemental new drug application for Casodex (bicalutamide) 150mg for early prostate cancer.

The FDA decision does not impact on the use and approval of Casodex 50mg formulation for advanced prostate cancer, the company said.

"Casodex 150mg is being evaluated in the largest ever treatment study in prostate cancer—the Early Prostate Cancer program," said Gerard Kennealey, vice president of oncology research at AstraZeneca. "The first results show that Casodex 150mg provides important benefits for early stages of prostate cancer. We want to fully review our options with the FDA to find the best way forward, including possibly requesting an advisory committee meeting. In addition, the FDA has suggested that we request a public hearing to review the data and discuss the findings in an open forum."

The 150 mg drug is approved for the treatment of early or locally advanced prostate cancer in 50 countries including the UK, Italy, Austria and Mexico, the company said.

The sNDA submission was based on the first results of the EPC program, which showed that adding 150mg dosage to standard care reduces the risk of tumor progression by almost a half and reduces the incidence of bone metastases by a third in patients with localized or locally advanced prostate cancer, compared with standard care alone, the company said.

AstraZeneca and FDA had a difference of opinion on the

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FTC Says Merger Would Limit Competition In Cancer Tests

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Joe Simons, director of the FTC Bureau of Competition. "As a result of the proposed acquisition, it is likely that prices would increase, product innovation would suffer, and ultimately, patient care would be compromised."

Both Cytyc and Digene manufacture and sell products used to screen women for cervical cancer, the company said. The Cytyc product accounts for 93 percent of U.S. liquid-based Pap tests. Liquid Pap tests are the most widely used sensitive primary screening tool available for the detection of cervical cancer. The only other company currently producing and selling an FDA-approved liquid Pap test in the U.S. is TriPath Imaging. While three other companies have developed such tests, they have not yet begun clinical trials, and are at least two years away from entering the U.S. market.

Digene is the only company in the U.S. selling a DNA-based test for the human papillomavirus, and it appears likely that Digene will continue in the position for the foreseeable future, the company said. PV viruses are believed to cause nearly all cervical cancer cases. Digene's HPV test is most commonly and efficiently conducted using a residual sample obtained from a liquid Pap test, but doing the test this way requires FDA approval. Thus, it is important that a company manufacturing liquid Pap tests have FDA approval to run the Digene HPV test off its sample medium. It is similarly important that a liquid Pap test supplier's customers have viable access to Digene's HPV test. By purchasing Digene, Cytyc would be in a position to eliminate its only existing competitor by limiting access to Digene's HPV test, and, in a similar manner, could also thwart the entry of other firms that have planned to begin selling liquid Pap tests in the United States in the near future.

The proposed acquisition also would eliminate future competition from the Digene HPV test itself, both in conjunction with Pap testing and later on a stand-alone basis to test for cervical cancer. Digene's HPV test is not currently used for primary cervical cancer screening in the United States, but rather as a follow-up test when Pap test results are unclear. However, it is anticipated that in the near future Digene's HPV test is likely to compete more directly with liquid Pap tests in the primary screening market. Digene has already applied for FDA approval for the use of the HPV test in conjunction with Pap testing as a primary cervical cancer screen, with final approval expected before the end of 2002. In addition, in the next four to five years, the FDA is expected to approve HPV testing as a stand-alone primary cervical cancer screening tool that could be used in lieu of Pap testing, particularly for women over the age of 30.

According to the FTC, the Cytyc proposed acquisition of Digene raises significant antitrust concerns. The market for sensitive cervical cancer screening tools is extremely concentrated, and in order to compete effectively, TriPath and its customers must have viable commercial access to the Digene HPV test. In addition, TriPath must have continued assistance from Digene in obtaining necessary FDA approvals to be used with the Digene current and next-generation HPV tests.

The Commission's complaint will allege that the Cytyc acquisition of Digene would eliminate or substantially reduce its only existing competition in liquid Pap testing, as well as the only competition it likely would face for many years. Several other firms have developed liquid Pap tests and plan to enter the market in the near future. If the proposed acquisition takes place, the complaint will contend, these firms are unlikely to receive cooperation from Cytyc/Digene in obtaining needed FDA approvals, and even if they do, they and their customers would be unlikely to have competitive access to the Digene HPV test.

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Additionally, the complaint will allege that, absent the acquisition, Cytyc faces future competition from the Digene HPV test in its own right. While the Digene HPV test is currently FDA-approved for use only as a follow-up test to equivocal Pap test results, the role of HPV testing is rapidly expanding into the much larger arena of primary screening - where Cytyc and its liquid Pap test lead the market. According to the FTC, HPV testing is the most likely technology to compete against liquid Pap testing as a primary cervical cancer screening tool in the future.

The action authorizes staff to seek a federal district court order to prevent Digene's proposed acquisition by Cytyc. The Commission has authorized staff to file a motion for preliminary injunction on the grounds that the transaction, as currently proposed, would violate federal antitrust laws. If the court grants the FTC's motion, the Commission will have 20 days to determine whether to issue an administrative complaint.

The Commission vote authorizing staff to seek a preliminary injunction was 5-0.

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Blue Cross and Blue Shield of St. Paul, Minnesota, said it has received approval from the Minnesota Department of Commerce for its $412 million health investment initiative.

The plan reduces premiums for many businesses, provides cost relief for qualified Blue Cross members, and slows the rate of increase in heath care costs, the company said.

Called "A Healthier Minnesota," the initiative will be funded entirely from the money tobacco companies are paying to Blue Cross as a result of a lawsuit, the company said.

"This closes the book on a remarkable journey Blue Cross began eight years ago when we became the first private health plan in the country to sue the tobacco industry," said Mark Banks, CEO of Blue Cross. "Not many people gave the lawsuit a chance, but Blue Cross stuck to its principles and ultimately won. Now we begin writing a new book—investing in a plan that will provide for a healthier place to live and work for all Minnesotans."

The centerpiece of the Blue Cross plan—an investment of $252 million in health improvement—did not require any regulatory approval, the company said.

"Blue Cross is committed to investing our tobacco proceeds in long-term comprehensive, science-based health improvement and prevention programs," Banks said. "We are committed to reducing the use of tobacco and creating long-lasting positive change in the health of our state."

* * *

BioVex Ltd. of Oxfordshire, England, has entered into an agreement with **GlaxoSmithKline** of Toronto in immunotherapy.

Under the agreement GlaxoSmithKline will evaluate the ability of the BioVex ImmunoVEX vaccine platform to break immune tolerance to chronic disease through the delivery of antigens to dendritic cells, the company said.

ImmunoVEX is a dendritic cell based vaccine platform, the company said.

"The ImmunoVEX agreement provides GlaxoSmithKline with an opportunity to evaluate a novel vaccine technology, which may prove to be one of the most potent means for delivering antigens to dendritic cells to stimulate an immune response against cancer and major chronic infectious diseases," said Gareth Beynon, CEO of BioVex.

Studies have shown that antigen presentation by the immune systems key policing cells—dendritic cells—can lead to a therapeutically effective immune response against disease associated antigens to which the body has become tolerant, the company said. The diseases include a broad range of cancers and infectious diseases such as those caused by HPV, HBV, HCV, HIV and malaria.

HSV infects and delivers antigen-encoding genes to dendritic cells at very high efficiency and could become one of the leading methods for loading these cells with antigen, the company said. Dendritic cells infected with HSV are usually in-activated by the virus; BioVex has identified the genes responsible for this inactivation. The deletion of these genes provides a proprietary vaccine platform which combines very efficient antigen delivery to, and optimal stimulation of, this class of antigen presenting cell, the company said.

BioVex is a private biotech company developing therapeutics for cancer and chronic infectious disease; it has two proprietary product platforms (OncoVEX and ImmunoVEX) and a functional genomics platform all based on the manipulation of the herpes simplex virus.

* * *

Iceland Genomics Corp. of Reykjavik said it would collaborate on a cancer gene discovery with **Myriad Genetics Inc.** (Nasdaq: MYGN).

Under the agreement, Myriad will supply

genetic markers and IGC will use them with its proprietary sample collection to help Myriad localize and identify the cancer gene, the company said. IGC will receive research support payments as well as milestone payments and royalties on any diagnostic or therapeutic products, which are developed by Myriad on the basis of the gene.

Financial details of the collaboration are undisclosed, the company said.

"This new collaboration with Iceland Genomics will make pinpointing the location of this new gene faster and more cost-effective," said Mark Skolnick, chief scientific officer of Myriad Genetics, Inc. "Genetically isolated populations, such as that of Iceland, are important to gene discovery because they simplify the tracking of variations through the population, compared with non-isolated populations," he said.

* * *

Lorus Therapeutics Inc. of Toronto said it has been approved by the Drug Development Group of the NCI Division of Cancer Treatment and Diagnosis to supply it with the antisense drug, GTI-2040, for multiple clinical trials to evaluate its efficacy in a range of cancers.

NCI selected GTI-2040 after an analysis of preclinical, GLP toxicology and phase I trial data, the company said. Lorus and NCI will work together to select cancer indications and development programs for a number of clinical trials. NCI will sponsor trials conducted with GTI-2040 alone or in combination with other cancer therapies. Lorus will manufacture and provide drug for all trials under the collaboration.

GTI-2040 is being investigated in a phase II trial in combination with capecitabine renal cell carcinoma, the company said. The phase II trial is being conducted at Wake Forest University under the supervision of Frank Torti, director, Comprehensive Cancer Center.

* * *

SignalGene Inc. (TSE:SGI) of Montreal and **Novuspharma SpA** (Nuovo Mercato: NOV.MI) of, Milan, Italy, said they have entered into a material transfer and option agreement in oncology.

Under the agreement, Novuspharma will conduct in vivo studies to determine efficacy against various cancers and preliminary safety studies of SG292, a compound from the SignalGene anti-angiogenesis program, the companies said.

In exchange for conducting the studies, Novuspharma will receive a time-limited option to negotiate exclusive rights to the SG292 compound for further preclinical and clinical development and commercialization in oncology indications, the companies said. All data resulting from the studies will become the property of SignalGene, which will retain the rights to SG292 for all other indications.

"Building on the positive results of our in vivo studies with SG292 in breast cancer, this agreement provides us with an excellent partner to pursue the further development of this compound for indications in cancer therapy," said George Masters, interim president and CEO of SignalGene.

Angiogenesis, the process which leads to the formation of new blood vessels, allowing tumors to grow, invade surrounding healthy tissue and ultimately become metastatic and spread through the body, the companies said. Studies have demonstrated that efficient inhibition of angiogenesis can block tumor growth in experimental models.

* * *

Theragenics Corp. (NYSE: TGX), of Atlanta said it has entered into a market development and distribution agreement with **Trace Sciences International Inc.** of Toronto for stable isotopes.

The agreement provides a framework under which Trace Sciences will perform market development and limited sales activities for stable isotopes to be agreed upon by Theragenics, the company said.

Enriched stable isotopes are purified forms of material with applications in aerospace, fuel, energy, manufacturing, defense, medicine and diagnostics, the company said.

Theragenics Corp. is the manufacturer of TheraSeed; a rice-sized device used in localized prostate cancer with a one-time, minimally invasive procedure, the company said.

* * *

TransTech Pharma Inc. of High Point, NC, and **Cephalon Inc**. (Nasdaq: CEPH) of West Chesterm, PA, said they have entered into a multi-year research collaboration using the TransTech proprietary translational technology to discover and develop small molecules for up to three therapeutic targets.

Under the agreement, Cephalon has the exclusive right to develop and commercialize all compounds directed at each of the targets covered by the collaboration, the companies said. TransTech would receive payments upon the achievement of specified research, clinical and commercialization

milestones. In addition, TransTech would receive royalties on future product sales. Specific terms of the agreement were not disclosed, the companies said.

The transTech translational technology is an automated and fully integrated drug discovery process including proprietary software modules, the companies said. The technology has shown promise against biological targets including protein-protein interactions, receptor modulators and enzyme inhibitors, and delivered small-molecule-based pre-clinical drug candidates for diabetes, cancer, inflammation, Alzheimer's disease and thrombosis, the companies said.

Product Approvals & Applications:

FDA Issues Non-Approvable Letter For Casodex

(Continued from page 1)

interpretation of the data and how it applies to patients, the company said. The EPC program was designed on the same premise as the adjuvant trials of tamoxifen for breast cancer. The program is the largest prostate cancer treatment study to date including over 8,000 patients from 23 countries.

"Casodex 150mg addresses a current unmet medical need in the treatment of prostate cancer," said Peter Iversen, one of the principal investigators of the Casodex EPC programme. "We have seen how hormonal therapies such as tamoxifen save lives in breast cancer patients, and the initial results from the EPC program give us hope that we will be able to offer similar benefits to men with early prostate cancer."

* * *

Amgen (Nasdaq: AMGN) of Thousand Oaks, CA, said the European Committee on Proprietary Medicinal Products has recommended approval of pegfilgrastim (Neulasta/Neupopeg) for the reduction in the duration of neutropenia and the incidence of febrile neutropenia in patients treated with cytotoxic chemotherapy for malignancy (with the exception of chronic myeloid leukemia and myelodysplastic syndromes).

The recommendation from the CPMP will be forwarded to the European Commission for its approval of the marketing authorization, the company said.

Neulasta is a long-acting form of filgrastim, which allows for once-per-chemotherapy cycle dosing, the company said. In addition to reducing daily injections, simple, once-per-chemotherapy- cycle administration of Neulasta may increase adherence to treatment regimens and eliminate the potential for missed doses of growth factor.

Neulasta is a pegylated recombinant protein that stimulates the production of neutrophils that are depleted by cytotoxic chemotherapy.

"This once-per-cycle product can have a very positive impact on patients' quality of life," said Martine Piccart, of the Institute Jules Bordet, in Belgium, an investigator in the fixed dose, pegfilgrastim study conducted in Europe.

Due to the relatively short time it remains circulating in the blood, filgrastim requires up to two weeks of daily injections following each cycle of chemotherapy, the company said. Almost half of chemotherapy patients who receive filgrastim require 10 or more daily injections. With Neulasta, a polyethylene glycol molecule or PEG unit is covalently bound to the filgrastim molecule, extending its half-life and causing it to be cleared more slowly from the body mainly through neutrophil and neutrophil precursor-mediated clearance mechanisms. This allows for a single dose per chemotherapy cycle.

Consistent with self-regulation through neutrophil-mediated clearance of Neulasta, the drug remains in the blood throughout the time during which a patient is neutropenic—when it is needed most—and then is cleared rapidly as neutrophils rise toward normal levels, the company said.

Data from two phase IIII studies in breast cancer patients demonstrated that a single dose of Neulasta provided protection from infection comparable to a median of 11 daily injections of filgrastim, reducing both the duration of severe neutropenia and the frequency of neutropenia with fever.

Clinical trials showed that Neulasta is as safe and well-tolerated as filgrastim, the company said. The most common adverse event was bone pain, which was reported in 26 percent of patients. In most cases, bone pain was mild to moderate, and controlled with non-narcotic analgesics.

New Products:

Proteome Systems Markets Software For Research

Proteome Systems Ltd. of Sydney, Australia, said it has released ProteomIQ, an integrated comprehensive solution that accelerates proteomics

research for cancer.

ProteomIQ brings together niche sample preparation and analytical technologies with enterprise level computing and extensive training and support programs to offer an end-to-end solution for proteomics research, the company said.

"The combination of separation technology, robotics, mass spectrometry and enterprise level computing is unique to ProteomIQ, which delivers comprehensive outcomes through its ability to decipher proteomic complexity," said Marc Wilkins, executive vice president, bioinformatics, Proteome Systems.

Alliances with partners such as IBM, Shimadzu Biotech, Millipore, Sigma-Aldrich and ThermoFinnigan enabled Proteome Systems to accelerate the development of ProteomIQ, the company said.

"Our technology has been developed by practitioners of proteomics, specifically for proteome research, and has been rigorously tested in our in-house projects in cystic fibrosis, cancer, infectious diseases and aging," said Keith Williams, CEO, Proteome Systems.

ProteomIQ includes is a patented technology for protein separation, analysis and informatics, which together delivers faster, more reproducible results, the company said. ProteomIQ produces data and assembles it into useful biological information for researchers. The technology is integrated through an informatics package that includes BioinformatIQ, a web-based intranet application that controls laboratory instrumentation and centralizes all research outcomes into an IBM DB2 database software hosted on IBM eServer pSeries systems.

"Proteome Systems has delivered a powerful solution for rapidly deciphering complex protein data," said Mike Svinte, vice president of Worldwide Business Development for IBM Life Sciences. "ProteomIQ brings together leading edge technologies, including an information technology infrastructure based on IBM eServer and DB2 data management systems, that will support proteomic research and scale to meet future requirements."

Oncology Management:
Network Appliance Wins Contract From OTN

Oncology Therapeutics Network said it would use the business continuance solutions for data management services from **Network Appliance Inc.** (Nasdaq: NTAP).

OTN, a subsidiary of Bristol-Myers Squibb, uses Network Appliance SnapMirror replication technology and NetApp F800 series filers to make real-time backups of its customer relationship and enterprise resource planning applications in the BMS New Jersey data center, the company said.

The Network Appliance SnapMirror offers disaster recovery via fast replication of mission-critical information, the company said. SnapMirror enables enterprises to mirror selected mission-critical data sets stored within a single volume for disaster recovery, data distribution, offline testing, and reporting. By mirroring selected data sets and transferring only changed blocks over the network, SnapMirror dramatically lowers network bandwidth requirements, the company said.

"Our goal is to make the oncology practice as efficient as possible by providing the oncologist with the best service through the latest technology," said Sue Dubman, vice president and CIO at OTN. "Using the business continuance solutions we are able to ensure the highest levels of data availability while offering personalized and absolutely secure service."

* * *

Impac Medical Systems Inc. of Mountain View, CA, and **US Oncology** of Houston said they have entered into a five-year agreement to deploy the Impac integrated oncology management system software in the over 75 comprehensive cancer centers operated by US Oncology, nationwide.

Impac was selected because of critical performance criteria, which includes the ability to manage advanced radiation treatments such as intensity modulated radiation therapy), an integrated electronic medical record with image management capability, and seamless integration with core business functions as scheduling, authorizations tracking, and charge management, the company said. In addition, the Impac system will act as the integration hub for treatment planning and delivery devices connecting equipment from multiple vendors—Philips Medical Systems, CMS, and Varian Medical Systems—directly to the Impac EMR.

Impac will also supply and support the computer and local and wide-area networking infrastructure as well as address all of the wide-area telecommunications requirements, the company said.

"From our inception over 12 years ago, our objective has been to provide integrated, clinical and

administrative information and process management solutions to cancer centers, regardless of organizational structure," said Joseph Jachinowski, Impac president and CEO.

* * *

CDC Solutions Ltd. of Philadelphia said **ILEX Oncology Inc.** (Nasdaq:ILXO) of Chippenham, UK, has selected the Ezsubs publishing suite from CDC Solutions for their electronic publishing and submissions to regulatory bodies.

ILEX has a marketed drug, Campath in the U.S. and Mabcampath in the European Union, and is advancing a pipeline of additional cancer compounds, the company said.

"EZsubs from CDC Solutions will afford us the ability to compile electronic regulatory submissions and internal reports more accurately and in a fraction of the time it formerly took us to do the work manually," said Michael Bernstein, senior director of regulatory affairs at ILEX. "Only CDC Solutions provided the ease of use, integration and support services, and implementation timeframe that fit into the overall objective of having a complete publishing solution in place quickly."

EZsubs is a highly scaleable publishing solution that supports electronic and paper outputs, and is designed to facilitate mission-critical reports and submissions to the European Medicines Evaluation Agency, U.S. FDA, and other regulatory bodies, the company said.

EZsubs works with an existing document management system or file system for reports, amendments, and regulatory submissions, the company said.

Clinical Trials:

BioVex To Begin Phase I Trial Of OncoVex GM-CSF

BioVex Ltd. said the Medicines Control Agency of the UK has approved a phase I trial for OncoVEX GM-CSF for tumors.

The 18-patient trial will take place at the Hammersmith Hospital in London and will be led by Charles Coombes, professor of oncology, Imperial College School of Medicine, the company said. The safety and biological activity of the treatment will be evaluated in a number of solid tumors including melanoma, breast cancer, gastro-intestinal cancer and head and neck cancer.

OncoVEX products are versions of herpes simplex virus, which have been engineered such that they replicate selectively in tumor cells, destroying the tumor in the process, the company said.

In addition to the anti-tumor effect provided by the oncolytic virus itself, OncoVEX GM-CSF carries the gene encoding human GM-CSF, which is an immune stimulator designed to stimulate the immune response to tumor cells, the company said.

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City of Hope Medical Center of Los Angeles and the **University of Alabama at Birmingham** said they have received approval to begin phase I/II trials of an investigational drug, 131I-TM-601, developed by **TransMolecular Inc**, of Birmingham, AL, for glioma.

The drug, 131I-TM-601 is a radiopharmaceutical containing a synthetic version of a substance derived from scorpions, called chlorotoxin, the companies said. The multi-center study will evaluate the safety and tolerability of a single dose of the drug, as well as overall tumor response rate in the initial study group of 18 patients.

In pre-clinical studies, 131I-TM-601 was able to extend survival in a mouse model that mimicked human brain tumors, the companies said. TM-601, based on chlorotoxin sequences, has been shown to be non-toxic in animal studies.

"Therapeutic options for glioma patients are rather limited," said Matthew Gonda, president and CEO of TransMolecular. "We have now harnessed the power of Mother Nature by incorporating a natural product into our anti-cancer drug. 131I-TM-601 uses sequences from chlorotoxin that have evolved to precisely locate and bind to their receptor, which is abnormally expressed on tumor cells, but not on normal cells. It's like molecular surgery. The chlorotoxin sequences are the guidance system that delivers a radioactive payload to its target, precisely killing the tumor cells."

Doctors at City of Hope Cancer Center and the UAB Brain Tumor Treatment and Research Program are seeking adult patients with recurrent glioma who have not had prior treatment with gene therapy, brachytherapy, radiosurgery or implants of polymers containing chemotherapeutic agents. Patients must also be eligible for resection of the recurrent tumor. Eighteen patients will be monitored over a six-month period during the study. Prospective patients or their physicians should contact UAB at 205-975-0438 or City of Hope at 626-359-8111, ext. 63033 or ext. 62329.

In another development, Genentech Inc. (NYSE: DNA) said it will appeal a Los Angeles County Superior Court jury award to **City of Hope** of $200 million in punitive damages. The company also said it will appeal the judgment in the case to the California Court of Appeal.

"We strongly disagree with the result in this case," said Arthur Levinson, Genentech chairman and CEO. "Genentech has lived up to the letter and spirit of the contract and paid the City of Hope everything it was entitled to under the 1976 agreement. We will appeal the judgment and have great confidence in our position."

Genentech will begin the post-verdict and appeals process immediately, the company said.

Under the long-held interpretation of the 1976 agreement in question, Genentech paid COH royalty payments on sales of products made using DNA produced by COH and that use the patented technology that resulted from the sponsored research, the company said. COH accepted the royalty payments, totaling more than $300 million, from Genentech for over 20 years without raising any question or concern about them.

COH filed the original contract dispute suit against Genentech in 1999, the company said. The first trial resulted in a hung jury, 7-5 in Genentech's favor, in October 2001. In the retrial, the jury deliberated for 17 days before announcing the verdict on June 10, which directed Genentech to pay about $300 million in additional royalties. The trial continued three days and the jury deliberated an additional three days before announcing the punitive damages award granted to COH.

The appeals process could take anywhere from one to four years depending on the scope of the review, the company said. Genentech will record a one time charge of about $500 million (compensatory and punitive damages) in the second quarter of 2002. This charge will hit the company's actual earnings but will not affect Genentech's pro forma earnings.

Genentech has posted the text of the original 1976 agreement, commentary from Levinson, and Genentech's and COH's interpretations of key sections of the contract on its website at *www.gene.com/gene/news/CEOperspectives/index.html.*

* * *

Coley Pharmaceutical Group Inc. of Wellesley, MA, said it has begun a phase I/II clinical trial of CpG 7909, as a monotherapy for stage IV melanoma.

The multi-center study will evaluate the safety and tolerability of weekly doses of the monotherapy, as well as overall tumor response rate in an initial study group, the company said. Additional patients will be enrolled to test drug efficacy.

"The trial is part of our two-pronged strategy to test CpG 7909 both as a monotherapy for treatment of cancers and as part of multidrug regimens, as in our ongoing trials of CpG 7909 with Herceptin for breast cancer and with Rituxan for non-Hodgkin's lymphoma," said Robert Bratzler, president and CEO off Coley Pharmaceutical Group.

"The therapeutic options for metastatic melanoma, such as chemotherapy and/or non-specific immunotherapy, are rather limited and very unsatisfactory," said Stephan Wagner of the University Clinic for Dermatology, General Hospital of the City of Vienna and principal investigator of the study. "Preclinical studies have shown that CpG 7909 alone promotes NK cell and Th1-biased T cell responses against cancer cells, including malignant melanoma, providing a scientific rationale for use of this novel immunostimulatory therapeutic strategy."

The General Hospital of the city of Vienna is one of the six European Union clinical sites participating in the study, the company said.

* * *

MGI Pharma Inc. (Nasdaq: MOGN) of Minneapolis said it has begun a phase I trial of irofulven, its anti-cancer compound, in combination with the anti-tumor drug Xeloda (capecitabine) for advanced solid tumors.

The primary objective of the dose-escalating trial is to determine the maximum-tolerated dose of the two drugs when used in combination, the company said. Secondary objectives are safety, anti-tumor activity, and the pharmacokinetic profile of irofulven and capecitabine when administered in combination. Up to 40 patients will be enrolled in the international, multi-center study. Irofulven will be administered intravenously on an every-other-week dosing schedule, and capecitabine will be administered orally every 12 hours.

"This is an important first clinical step in determining the chemotherapeutic role of irofulven in combination with capecitabine, a prodrug that is converted to 5-fluorouracil (5-FU) in tumors," said Jerome Alexandre, assistant professor at Hopital Cochin in Paris, France, and PI for the trial.

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