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Lung Screening Study Ties Up Advisors, Board Sends It Back To NCI For Revision

In a tie vote, the NCI Board of Scientific Advisors neither approved nor killed outright the Institute's plan for a randomized, controlled trial of lung cancer screening comparing spiral CT vs. chest x-ray.

With 24 of 35 board members in attendance at its July 25 meeting, the board voted 12-12 on a motion to approve the proposed Lung Screening Study II.

While a faction of the board opposed the study outright, a majority agreed that NCI's proposal needed rethinking. The board formed a

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In Brief:

Wong To Head MSKCC Colorectal Service; How You Know When To Stop Advising NCI

W. DOUGLAS WONG was named chief of the colorectal service in the Department of Surgery at Sloan-Kettering Cancer Center by **Harold Varmus**, president of MSKCC and **David Golde**, physician-in-chief. Wong, who continues to serve as co-leader of the colorectal disease management team, is a surgeon whose research interests include endorectal ultrasonography. . . . **VIRGINIA ERNSTER**, member of the NCI Board of Scientific Advisors since the board's formation in 1996, stepped down from the board this week, a few months before her term ended. NCI Director **Richard Klausner** gave her the Director's Service Award for outstanding service to the Institute. Ernster has announced her retirement as professor of epidemiology and associate director for epidemiology, prevention, and control at the University of California, San Francisco, Cancer Center. "I go 24/7 for weeks on end just like everybody else, but I can't fit in the music, and working with hospice, and seeing the occasional sunset, and all of those things that I yearn to do," she said to the board this week. "But if a Klausner pathway had been identified where we could do 48/7 or 72/7, maybe I would have made a different decision." Ernster is a veteran traveler to Bethesda, having previously served on the former Boards of Scientific Counselors of the former NCI Division of Cancer Etiology and the Division of Cancer Prevention and Control, as well as dozens of other NCI committees. "After a while, you all become our network of colleagues and our understanding of how truly multidisciplinary cancer research is, so I want to thank you and wish you all godspeed," she said to the board and NCI staff. "I figured out this morning how you know when your time has come, and that is when you have been a guest in every single room of the Hyatt Regency Bethesda."

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Board Tells NCI To Revise Lung Screening Study

(Continued from page 1)

subcommittee to help NCI revise the study for resubmission to the board for an email vote sometime before the board's next meeting in November.

The study proposes to randomize 15,400 long-term smokers to spiral CT or chest x-ray to test the hypothesis that lung cancer mortality will be reduced by 50 percent or more by spiral CT.

NCI estimated the trial would cost $52.6 million over five years.

"The ticket is very large," conceded Robert Wittes, NCI deputy director for extramural science.

Board members encouraged the Institute to seek funds from other sources, including other countries that may be interested in joining the study. The Institute is feeling a budget crunch as a result of the expanded grant commitment base and the rising expectations of researchers over several years of large increases in appropriations.

With the prospect of smaller budget increases in coming years, NCI officials needed strong support from the advisory board to move ahead with the study. The board appeared split between the enthusiastic to lukewarm supporters of the study, and those who strongly opposed it.

Spiral CT, a new technology, is marketed as a screening method that works better than chest x-ray, but neither screening method has been proven to reduce lung cancer mortality.

The Mayo Lung Project tested chest x-ray and sputum every four months vs. a recommendation for an annual chest x-ray. The trial found that participants who were screened had longer survival after diagnosis, but there was no reduction in lung cancer mortality.

No endpoint data are available yet for NCI's Prostate, Lung, Colorectal and Ovarian cancer screening trial. In the trial, begun in the early 1990's, 154,000 participants with a mixed history of smoking were randomized to chest x-ray or usual care.

Enthusiasm for spiral CT emerged in 1999 when Claudia Henschke, professor of Radiology at Weill Medical College of Cornell University, reported in the Lancet the results of the Early Lung Cancer Action Project, a single-arm study of spiral CT and chest x-ray in heavy smokers. In the study, more cancers and non-calcified nodules were found with spiral CT than chest x-ray.

In October 1999, an NCI workshop endorsed a randomized controlled trial of spiral CT screening for lung cancer. Last year, NCI carried out a pilot project to test the feasibility of such a study. The Lung Screening Study I, conducted as part of PLCO, randomized more than 3,000 participants in two months. Participants had to be 55-74 years old, current smokers or had quit within 10 years, with 30 pack-years history of smoking, and no chest CT in the last two years.

The pilot study showed that a larger trial is possible, and could be completed by 2005, said John Gohagan, of NCI's Division of Cancer Prevention, who presented the concept to the board. The LSS II would be done by contract.

Stakes Are High, Treatment Progress Slow

Board member William Wood led the faction of the board that strongly favored the study. "The stakes are huge—this is the No. 1 killer," said Wood, professor and chairman of surgery at Emory University School of Medicine. "We are not dazzlingly effective in lung therapy. If this is effective, you could apply this to 20 million people."

Wood moved that the board approve the concept and encourage NCI to increase the sample size in order to detect a 20 percent reduction in mortality.

"Progress has been extremely slow in treatment," said board member Waun Ki Hong, chief of cancer medicine at M.D. Anderson Cancer Center. "This is a trial one can do in our lifetime."

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"The need is great and the impact would be tremendous," said board member John Minna, director of the Hamon Center for Therapeutic Oncology Research, University of Texas Southwestern Medical Center. "Spiral CT is sweeping the country now. However, it is sweeping the country only for the upper incomes."

The concept does not address who will pay for follow-up biopsies and treatment for participants who don't have insurance coverage, Minna said. Also, the study should include linkage with genetic epidemiology. "I'd like to see this proposal come back with these things tightened up," he said. "The end result might be an even bigger trial."

"This trial is not big enough at the outset," said Robert Young, president of Fox Chase Cancer Center. "Four to five years from now, it will be even more expensive to do this trial. This is the time to do it."

Leading off from the opposing camp was David Abrams, director of the Center for Behavioral and Preventive Medicine, Brown University. "I'm not that excited about a head-to-head test of what I think is a straw person, x-ray vs. spiral CT as the major arm of a study like this," Abrams said. "It's pretty clear to me already that if you do spiral CT and x-ray on the same person, which reduces the inter-person variability and is a better way to look at head-to-head sensitivity and specificity, you've got far better detection than spiral CT.

"I think the more exciting opportunity right now is to design a study that maximizes the morbidity-mortality outcome by all means of intervention," Abrams said. "I'd be far more interested in early detection screening as a new population motivator for both detecting early lesions and beginning to think about maximizing an intervention that would go something like either minimal or no treatment, CT alone, CT alone plus aggressive smoking cessation plus all other ideal therapies.

"I'm not saying that would be the ultimate design, but I'm putting out an alternative way to look at how you might start looking at combined intervention to reduce mortality that would capitalize on spiral CT for early detection," Abrams said. "Simply moving us faster toward combined intervention would have a dramatic influence on morbidity and mortality."

"I'm really opposed to this trial," said Barbara Weber, professor of medicine and genetics, University of Pennsylvania Cancer Center. "[Lung cancer] is 90 percent preventable and we know how to do it. This technology can only increase over time the cost of smoking on health care in the U.S."

"It's not true that 90 percent of lung cancer is preventable," said NCI Division of Cancer Prevention Director Peter Greenwald. "Given where we are today, about half of lung cancer is occurring in former smokers, so addressing prevention of smoking will do nothing for them."

Greenwald said Abrams' proposal of including other interventions would increase costs substantially. Also, he said, NCI calculated that to detect a 20 percent decrease in mortality, the trial would have to enroll 60,000 people.

"Train Is Out of The Station"

"I think the train is so far out of the station with this technology that were the benefits and harms not established, I think there would be a greater harm to not going ahead with the trial and an adequately powered trial, and doing it while we have the window of opportunity," said Virginia Ernster, professor of epidemiology and genetics, University of California, San Francisco, Cancer Center. "David, of course your scenario is an ideal one, but I think it would be way, way too expensive."

Board members wondered whether tobacco settlement funds could be used for the study, but Young noted that most states have already allocated the funds.

"If it would help with the funding, I'd be happy to contribute the $300 I got in a property tax rebate from the state of Illinois [from the settlement]," said Richard Schilsky, associate dean for clinical research, University of Chicago.

"I really come down on the side of the argument that Bob Young advanced," Schilsky said. "We have only one opportunity to do this and do it well, and right now you can walk into any hospital in America and plunk down your $350 or $400 and get a spiral CT scan and nobody knows how to interpret the results. The potential costs to the health care system are enormous until we pin down the value of this.

"If we're going to do this, it has to be done right," Schilsky said. "It has to be a larger study with better statistical power, early stopping rules, and an independent data and safety monitoring board."

"Train Is All The Way Down the Hill"

"I'm afraid that no matter what you do, the train is all the way down the hill and you're not going to catch it, in fact, you are just going to be adding momentum to the train by supporting a trial of the

kind of technologies that are running through the community," said Tom Curran, chairman of developmental neurobiology, St. Jude Children's Research Hospital.

"Looking at the cost projections, good arguments for adding on biomarkers, genetics, I think you're looking more like a quarter of a billion dollars for a substantial study," Curran said. "I wonder what would happen if you used that quarter of a billion dollars to come out with true therapies."

Greenwald: "The issue is mortality, not survival. There are people here who are better at describing therapies. Historically, we have not seen great improvement. There are potentially things that all have to be tested in trials, and those trials all will take at least five years after they get started, so we'd be way down the road."

Curran: "There's a lot of excitement about targeted therapies. I would be very sad if, in the lung cancer area, those new approaches couldn't be applied because all the money was tied up—."

Greenwald: "When do you think the next therapies will be in clinical trials and how long do you think the trials will take?"

Curran: "How long was STI571 [in trials]?"

Multiple Motions and Tie Vote

After about an hour of discussion, the board turned to points of order.

Wood's motion to approve the trial was on the table. Hoda Anton-Culver, professor and chief of epidemiology, University of California, Irvine, made a motion to table Wood's motion and form a committee to help NCI revise the concept.

The board voted 15-8, with one abstention, to approve Anton-Culver's motion, failing by one vote to achieve the two-thirds majority required to override a board member's motion.

The board then voted 12-12 on Wood's motion. Board Chairman Frederick Appelbaum did not call for a revote.

Anton-Culver reintroduced her motion to form a committee to revise the concept. The motion was approved 21-2, with one abstention.

Appelbaum, director of clinical research, Fred Hutchinson Cancer Research Center, appointed the following to a committee to work on the concept: Wood, Hong, Minna, Abrams, Schilsky, Alice Whittemore (Stanford University) and Amy Langer (National Alliance of Breast Cancer Organizations). Wood agreed to chair the committee.

Advisors Approve Program To Link Radiation Oncologists

The NCI Board of Scientific Advisors unanimously approved NCI's plan to spend $21.3 million over the next five years to support partnerships in radiation oncology between institutions that care for medically underserved, ethnic, and minority populations and are not involved in research with institutions that are significantly involved in research.

The program was proposed by Norman Coleman, director of the NCI Radiation Oncology Sciences Program. The board had asked Coleman at a previous meeting to revise and resubmit the concept.

Following are excerpts from the concept statement:

Cancer Disparities Research Partnerships: Concept for a new RFA, first year set-aside $3.2 million, anticipated total cost $21.3 million, six awards. Program director: Frank Govern.

Institutions providing health care services to a disproportionate number of medically underserved low income and/or minority populations, whether urban or rural, may not be linked to the national cancer research enterprise as effectively as they could be and often struggled to maintain state-of-the-art cancer care.

As a consequence, radiation oncologists in these institutions have difficulty in starting, developing, and sustaining research programs either independently or collaboratively.

Thus, the populations that these institutions primarily serve, largely minority, ethnic, and/or low income, do not readily benefit from the rapid progress being made in cancer research, and bear an unequal burden of disease.

The challenge for NCI is to assist these institutions and their radiation oncologists to the point of becoming active ineffective participants and partners in cancer research and clinical trials, leading to the improvement in the diagnosis and treatment of cancer and the reduction of health disparities among different segments of the American population.

This concept defines medically underserved populations as those having inadequate access to, or reduced utilization of, radiation oncology and multi-modality clinical research trials at their medical institutions.

The populations targeted by this program tend to access the health-care system in the advanced stages

of their disease and, because of this, radiation oncology usually represents a major treatment alternative. Therefore, the field of radiation oncology represents a unique opportunity to explore ways to improve cancer-related health disparities due to its technological base, the facility of application, and the ease of expansion into medical and surgical oncology. Because of its highly technical nature, radiation oncology is more amenable to field training approaches and network arrangements.

This proposal is targeting health care institutions that have adequate radiation facilities but 1) may only be minimally participating in NCI-sponsored clinical trials (1 percent or less of patient base is enrolled per year) or 2) are not currently participating in NCI-sponsored clinical trials.

Thus, these institutions, when provided necessary resources enclosed partnering with an institution experienced in cancer research, represent an opportunity for conducting and/or expanding participation in clinical trials developed for radiation oncology and combined modality therapy.

The CDRP program's overarching goals are to foster the development of independent clinical trials research in these institutions and is to develop the infrastructure for ongoing collaborative participation in radiation oncology research nationally.

CDRP is to facilitate the development of supportive and mentoring partnerships between institutions that traditionally provide care to medically underserved, ethnic, and minority populations, but have never been significant participants in the NCI biomedical research enterprise with those institutions that are active and committed participants.

Through partnerships, new centers, regions and segments of the population experiencing cancer related health disparities are brought to the research table. CDRP is to help institutions develop into capable and long-term participants in clinical research and high-quality treatment by funding infrastructure for clinical trials and assisting in the development of training and mentoring relationships with cancer experts in the region.

The program is built upon the experience in the Radiation Oncology Sciences Program to help grantees build an infrastructure environment for clinical research and improved care. CDRP is proposed as a demonstration project with metrics using a five-year competitive grant mechanism containing a "sunset" clause.

Well before "sunset," it is anticipated that the grantees will have established long-term working relationships with cancer research entities of their choice, such as NCI cancer centers and cooperative groups. CDRP will assist the respective grantee in implementing their partnership arrangements from the start of the grant as well as working with NCI cooperative groups and comprehensive cancer centers to develop sustained supporting relationships between these CDRP institutions and their partners.

CDRP will assist the grantees to arrange access to ongoing continuing education and training programs in radiation oncology that will help to ensure state-of-the-art delivery of their services. The program will promote the grantees' continued participation in research encompassing the highest standards of care in radiation oncology.

Through the ongoing support and mentoring of the partner, it is anticipated that the grantee institution will become a full participant in national training, education, and research programs.

For determining eligible institutions, the specific populations experiencing health disparities in the U.S. are defined as African-Americans, Asians, Pacific Islanders, Hispanics, Latinos, Native Indians, Native Alaskans, and/or those with low socioeconomic status as defined by the federal poverty level or the state defined level, if lower.

The program will use the U56 cooperative planning grant mechanism and will provide support for:

1. Administrative core activity (not to exceed 20 percent of the total direct costs) for salaries for key personnel, equipment and supplies to support and administrative structure, ongoing yearly support to the partnership institution for time, effort, and other resources expended in working with and mentoring the grantee.

2. Planning and evaluation core activities that may include the costs for travel for key personnel, and travel and per diem for members of the program steering committee, workshops, seminars, retreats, and other forums.

3. Developmental core funds for pilot research projects or pilot programs in research, training or career development, education and outreach; resources and infrastructure; support for research assistants or faculty; some salary support for investigators.

Cancer Risks:

IARC Finds Limited Evidence That Residential Magnetic Fields Raise Leukemia Risk

A working group of the Monographs Programme of the International Agency for Research on Cancer has concluded its review of health effects of static and extremely low frequency electric and magnetic fields.

Such fields include the earth's magnetic field, and also originate from electrical power transmission lines, electrical wiring in buildings, and electric appliances. Magnetic fields are measured in units of microTesla; the earth's static magnetic field, to which everyone is exposed, varies from 25 microTesla at the equator to 65 microTesla at the poles. Most research on health effects has been done on ELF magnetic fields with frequencies of 50 or 60 Hz.

Reports were first published in 1979 that childhood cancer might be associated with exposures to residential ELF fields. Numerous studies in many countries have been undertaken since then of possible increased cancer risks in children and adults from ELF magnetic field exposures.

Special attention has focussed on leukemia and on brain tumors, which early reports had suggested might be increased.

IARC has now concluded that ELF magnetic fields are possibly carcinogenic to humans, based on consistent statistical associations of high level residential magnetic fields with a doubling of risk of childhood leukaemia. Children who are exposed to residential ELF magnetic fields less than 0.4 microTesla have no increased risk for leukemia. Because of insufficient data, static magnetic fields and static and extremely low frequency electric fields could not be classified as to carcinogenic risk to humans.

However, pooled analyses of data from a number of well-conducted studies show a fairly consistent statistical association between a doubling of risk of childhood leukemia and power-frequency (50 or 60 Hz) residential ELF magnetic field strengths above 0.4 microTesla. In contrast, no consistent evidence was found that childhood exposures to ELF electric or magnetic fields are associated with brain tumors or any other kinds of solid tumors. No consistent evidence was found that residential or occupational exposures of adults to ELF magnetic fields increase risk for any kind of cancer.

Studies in experimental animals have not shown a consistent carcinogenic or co-carcinogenic effects of exposures to ELF magnetic fields, and no scientific explanation has been established for the observed association of increased childhood leukemia risk with increasing residential ELF magnetic field exposure.

Health effects of radiofrequency electromagnetic fields, which are produced by such sources as radio and television transmission towers, portable telephones, and radar, were not evaluated by the IARC working group. These exposures will be reviewed by the IARC Monographs Programme when research that is currently in progress has been published, most likely in 2005.

For further details of the Monographs evaluation, consult http://monographs.iarc.fr under "Agents most recently evaluated," or inquire by e-mail to cie@iarc.fr. For further details of current research at IARC on electric and magnetic fields, inquire by e-mail to cardis@iarc.fr.

Funding Opportunities:

Race for the Cure Grants For National Capital Area

Application Deadline: Aug. 17, 2001

Susan G. Komen Breast Cancer Foundation National Race for the Cure is offering grants for innovative, non-duplicative projects for non-profit organizations in the National Capital Area.

Only services conducted within and serving residents of the following areas will be considered for funding: Washington, DC, Montgomery County, Prince George's County, Fairfax County, Loudoun County, Arlington County, Alexandria City, and Prince William County. Grants are available for up to one year for a maximum $75,000.

Applications that may be considered include those aimed at increasing accrual to breast cancer clinical trials. Komen Affiliate Network is encouraged to enhance the capacities of NCI-approved clinical trials in a program called CRAFT (Clinical Research-Affiliates Fund Trials). CRAFT is a community grant-making program intended to increase participation in breast cancer prevention, treatment, and diagnostic clinical trials. The specific aims of CRAFT are to: provide community outreach and education about clinical trials; enhance community health care providers' participation and knowledge about trials; support institutional needs through infrastructure support, salary support and supplemental research;

address patient needs with costs and expenses associated with clinical trials participation.

A grant writing workshop will be held in Washington, DC on July 12, 8 a.m.-4 p.m., at Suburban Hospital, 8600 Old Georgetown Rd, Bethesda, MD. For information about the workshop fax Alicia Peterson 972-855-1640.

Applicants must register electronically via the Komen Foundation Web site on the Grant and Funding page, before submitting an application. Following registration, you will be assigned a tracking I.D. Number and receive a confirmatory email. All applications must have a Tracking I.D.#, which must be on all hardcopy pages of your application.

Inquiries: For MD counties not listed phone Maryland Affiliate at 410-963-0104; for VA counties not listed phone Greater Richmond Affiliate at 804-553-8718.

For additional information: Susan G. Komen Foundation, phone 888-300-5582; Web site http://www.komen.org.

AACR Grant Programs

Professorship in Basic Cancer Research

Nominations Deadline: Sept. 10, 2001

American Association for Cancer Research is accepting nominations for a senior scientist at the level of associate professor or professor in basic cancer research. The professorship will provide a two-year grant of $50,000 per year in salary support to promote research productivity of the recipient.

Cancer Research Fellowships and Career Development Awards

Application Deadline: Nov. 1, 2001

AACR invites applications from postdoctoral or clinical fellows for the 2002 research fellowships and from the assistant professor level for the career development awards.

—Gertrude B. Elion Cancer Research Award promotes basic, translational, or clinical cancer research by a non-tenured, tenure-tracked scientist at the level of assistant professor. The one-year award carries a grant of $50,000. Candidates must have completed postdoctoral studies of clinical fellowships no later than July 1 of the award year (2002) and ordinarily not more than five years earlier.

—Career Development Awards in Cancer Research are two-year awards of $50,000 per year for non-tenured, tenure-track scientists, at the level of assistant professor. At the time of application, candidates must be in the first or second year of a full-time, tenure-tracked faculty appointment at the rank specified earlier.

—Research Fellowships provide one-year grants of $30,000 to early career scientists in basic, translational, and clinical cancer research. Five fellowships will be awarded in 2002 to support salary and benefits for postdoctoral and clinical fellows. Candidates must have been a fellow for two years (since July 2000) but not more that five years (since July 1997) prior to the beginning of the award year.

Inquiries: AACR Web site http://www.aacr.org.

NIH RFA Available

RFA-TW-02-005: International Tobacco and Health Research and Capacity Building Program

Letter of Intent Receipt Date: Sept. 4, 2001

Application Receipt Date: Oct. 26, 2001

The RFA solicits research and capacity building projects that address the burden of tobacco consumption in low- and middle-income nations by 1) pursuing observational, intervention and policy research of local relevance and 2) building capacity in these regions in epidemiological and behavioral research, prevention, treatment, communications, health services and policy research. The overall intent of the program is to encourage transdisciplinary approaches to the international tobacco epidemic to reduce the global burden of tobacco-related illness. The program is designed to promote international cooperation between investigators in the U.S. and other high-income nation(s) pursuing research programs on tobacco control, and scientists and institutions in low- and middle-income nation(s) where tobacco consumption is a current or anticipated public health urgency. This RFA will use the NIH individual research grant R01 award mechanism. The RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-TW-02-005.html.

Inquiries: For NCI—Michele Bloch, Tobacco Control Research Branch, Behavioral Research Program, Division of Cancer Control and Population Sciences, NCI, 6130 Executive Plaza Blvd., Rm 4032, Bethesda, MD 20892, phone 301-496-8584; fax 301-496-8675; e-mail blochm@mail.nih.gov.

Program Announcements

PA: Cohort Studies in Cancer Epidemiology

NCI announces an annual receipt date for large investigator-initiated grants from investigators intending to competitively renew, competitively supplement, or initiate epidemiologic cohort studies of human cancers.

Integrating, prioritizing, and funding epidemiologic cohort studies has become an issue for NCI. Issues of key interest to the institute with regard to these

population resources include continuity of funding, balance of important cohort characteristics, quality of design, rigor of exposure assessment, level of response and follow-up rates, biospecimen collection and storage, bioinformatics, availability of biospecimen resources to outside qualified investigators, and other areas. Over time, it also may become necessary to limit cohort development in some areas and encourage it in others.

Because of constraints on the NCI budget resulting from the existence of numerous epidemiologic cohort studies, and the necessity for consistency in the review of these large projects, NCI has decided to accept applications in response to an annually issued PA. The PA is available at http://deainfo.nci.nih.gov/concepts/TPA-01-110.htm.

Inquiries: Sandra Melnick, Analytic Epidemiology Research Branch, Epidemiology and Genetics Research Program, NCI Division of Cancer Control and Population Sciences, phone 301-435-4914; email sm33k@nih.gov.

Cancer Prevention, Control, Behavioral and Population Sciences Career Development Award

NCI Cancer Prevention, Control and Population Sciences Career Development Award K07 supports cancer prevention, cancer control and the behavioral and population sciences as they relate to cancer. The target candidates are junior investigators with doctoral degrees or professional degrees (including doctorally prepared oncology nurses) who have a teaching or research appointment in the sponsoring institution. Information is available at http://deainfo.nci.nih.gov/concepts/canprevcontrol.htm.

Inquiries: Brian Kimes, Cancer Training Branch, Centers, Training and Resources Program, NCI, 6116 Executive Blvd. MSC 8346 Suite 7025, Bethesda, MD 20892-8346, phone 301-496-8580; fax 301-402-4472; e-mail bk34t@nih.gov.

PAR-01-110: Specialized Programs of Research Excellence in Human Cancer for 2002

Letter of Intent Receipt Dates: breast and gynecological cancer SPOREs: Dec. 1, 2001; lung, leukemia, and myeloma cancer SPOREs: April 1, 2002; prostate and genitourinary cancer SPOREs: Aug. 1, 2002

Application Receipt Dates: breast and gynecological cancer SPOREs: Feb. 1, 2002; lung, leukemia, and myeloma cancer SPOREs: June 1, 2002; prostate and genitourinary cancer SPOREs: Oct. 1, 2002

The Organ Systems Branch of the Office of the Deputy Director for Extramural Science at NCI invites grant applications for specialized programs of research excellence in organ-specific cancers.

A SPORE must develop and maintain human cancer tissue resources for the particular organ-site that will benefit translational research; promote extended collaborations in critical areas of research need with laboratory and clinical scientists within the institution, as well as in other institutions; and participate with other SPOREs on a regular basis in sharing positive and negative findings, assessing scientific progress in the field, identifying new research opportunities, and promoting inter-SPORE collaborations.

A SPORE is supported through the specialized center P50 grant mechanism, which provides funding for a broad range of research and developmental activities, from basic to human intervention studies.

The PA is available at http://grants.nih.gov/grants/guide/pa-files/PAR-01-110.html.

Inquiries: Jorge Gomez, (Leukemia, Myeloma, Prostate, and Genitourinary SPOREs, chief, email jg1w@nih.gov. Linda Weiss, (Lung SPOREs), program director, email lw187q@nih.gov. Jane Fountain, (Breast and GYN SPOREs), program director, email jf227t@nih.gov. Organ Systems Branch, Office of Centers, Training, and Resources, Office of Deputy Director for Extramural Science, NCI, 6116 Executive Blvd, Suite 7013, MSC 8347, Rockville, MD 20852 (for express/courier service), Bethesda, MD 20892-7008 (for U.S. Postal Service), phone 301-496-8528; fax 301-402-5319.

RAPID Program Date Change

Rapid Access to Preventive Intervention Development—Addendum

The receipt date for requests for RAPID resources has been changed to Oct. 1, 2001. Investigators are further notified that the contact person and Web site for the RAPID program have changed, see http://cancer.gov/rapid.

The program makes available to academic investigators the preclinical and early clinical drug development contract resources of the NCI Division of Cancer Prevention to move novel molecules and concepts from the laboratory to the clinic for clinical trials of efficacy. RAPID will assist by providing any (or all) of the preclinical and phase I clinical developmental requirements for phase II clinical efficacy trials. These include: preclinical pharmacology, toxicology, and efficacy studies; bulk supply, GMP manufacturing, and formulation; and regulatory and IND support and phase I clinical studies. Suitable types of agents for may range from single chemical or biological entities to defined complex mixtures to prevent, reverse, or delay carcinogenesis. See http://cancer.gov/rapid.

Inquiries: RAPID Program, Attn: Emilia Richichi, Chemopreventive Agent Development Research Group, Division of Cancer Prevention, NCI, Executive Plaza North, Rm 2117, 6130 Executive Blvd., Rockville, MD 20852 (overnight mail), 9000 Rockville Pike, Bethesda, MD 20892 (regular mail), phone 301-594-1165; fax 301-402-0553; e-mail richichi@mail.nih.gov

THE CANCER LETTER

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Business & Regulatory Report

Formerly "Cancer Economics"

Deals & Collaborations:

Bristol-Myers Squibb To Purchase DuPont Pharmaceuticals For $7.8 Billion

Bristol-Myers Squibb Co. (NYSE: BMY) said it would acquire the **DuPont Pharmaceuticals Co**., a subsidiary of **DuPont** (NYSE: DD), for $7.8 billion in a cash transaction.

"This acquisition is an important step in aggressively implementing our growth strategy, which envisions expanding our medicines business through acquisitions, joint ventures, licensing and co-promotion agreements, as well as through our own intensive and productive research and development efforts," said Peter Dolan, president and CEO of Bristol-

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Oncology Management:

Firm's Information System Embedded In iKnowMed For Treatment Outcomes

Actuate Corp. (Nasdaq:ACTU), of South San Francisco said its information delivery system was embedded in the iKnowMed Reporting Center, a reporting tool that lets practices monitor their clinical and financial performance, and view benchmark reports from the Network as a whole.

The iKnowMed Reporting Center, as delivered by the Actuate Information Delivery solution, presents blinded data from the iKnowMed Network, on treatment outcomes.

These outcomes include treatment response, toxicities, treatment regimen selection, relative dose intensity, chemotherapy dosing, and population overview. The Actuate reports can be generated and viewed with parameters defined by the user, the company said.

* * *

Apollo Telemedicine Inc., of Falls Church, VA, said the University of Pennsylvania Health Systems will use the company's eHealthStat telediagnostic network to improve imaging applications and services to domestic and international patients.

Apollo develops, assembles and markets patented telepathology systems. Last year, the company launched eHealthStat, a telediagnostic network, which follows a subscription based ASP model and enables healthcare professionals to provide diagnostic services via a TCP/IP based network.

* * *

InSiteOne of Wallingford, CT, a provider of Web-enabled onsite

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PO Box 9905
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Bristol-Myers To Purchase DuPont Pharmaceuticals Co.

(Continued from page 1)

Myers Squibb.

Last year, DuPont Pharmaceuticals realized sales of $1.5 billion, the company said. Promising compounds include a selective estrogen receptor modulator for breast cancer, agents affecting cellular processes associated with inflammatory diseases, and a selective receptor modulator for the treatment of obesity.

BMS said it would record a one-time, in-process R&D write-off and restructuring liability in the range of $2 billion to $3 billion.

Richard Lane, president, Worldwide Medicines Group, and executive vice president, Bristol-Myers Squibb, will oversee the integration of DuPont Pharmaceuticals and BMS, the company said.

Rick Winningham, president, immunology and oncology, and global marketing, BMS Worldwide Medicines Group, will manage the integration team, reporting to Lane.

* * *

Aastrom Biosciences Inc. (Nasdaq: ASTM) of Ann Arbor and **Neoprobe Corp.** (OTC Bulletin Board: NEOP) said they have entered into a collaboration agreement for an immune system cell therapy product for cancer.

The Neoprobe proprietary lymph node lymphocyte cell technology will be integrated with the patented AastromReplicell System and lymphocyte production technologies to produce a clinically usable cell therapy product, the companies said.

* * *

AltaRex Corp. (TSE: AXO, OTC: ALXFF) of Waltham, MA, said it has signed a memorandum of understanding with **Epigen Inc**. of Rochester, NY, to collaborate on research and development of antibody based treatments for twelve cancers associated with the human carcinoma antigen.

Epigen brings its proprietary human carcinoma antigen to the venture, the company said. HAC appears in circulation in early stage disease and is associated with the vast majority of epithelial cancers including prostate, ovarian, breast and non-small cell lung cancers, the company said.

AltaRex brings its proprietary dendritic cell assay to evaluate which of the Epigen foreign antibodies are capable of inducing beneficial immune responses, particularly T cell responses, against the target antigen HCA, the company said.

AltaRex said it is contributing a license to its key intellectual property related to its ability to elicit immune system responses against a targeted antigen in circulation.

Both companies said that a foreign antibody against HCA should elicit a multi-epitopic response and alter immunity to this self- antigen.

AltaRex said it had received a U.S. patent for the multi-epitopic method of treatment for OvaRex Mab and expects that all five antibodies in its cancer product portfolio, as well as the new Epigen antibody, will be operative under the same mechanism.

* * *

Cephalon Inc. (Nasdaq: CEPH) of West Chester, PA, said it has granted rights to market, sell and distribute ACTIQ (oral transmucosal fentanyl citrate), an opioid therapy for breakthrough cancer pain and other chronic pain, to **Orphan Australia**, a privately owned pharmaceutical company based in Melbourne, for Australia and New Zealand.

ACTIQ is marketed in the U.S. by Cephalon and in the U.K. through Elan Pharma Ltd.

The drug is available via the Cephalon patented oral transmucosal drug delivery system, the company said.

"The agreement with Orphan Australia is in line with our goal of building the global ACTIQ franchise through a dedicated network of effective partnerships," said Frank Baldino Jr. chairman and CEO of Cephalon.

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"There are now 22 international territories for which we have partnerships dedicated to the launch of ACTIQ."

* * *

ChromaVision Medical Systems Inc. (Nasdaq: CVSN) of San Juan Capistrano, CA, a provider of automated cell-imaging systems, said **Sugen Inc.** of South San Francisco, a subsidiary of **Pharmacia Corp.** (NYSE: PHA) of Peapack, NJ, has selected its automated cellular imaging system in its clinical development and cancer drug discovery programs.

Peer-reviewed clinical data and publications have demonstrated that ACIS is able to improve the accuracy, sensitivity, and reproducibility of cell imaging, the company said. Unlike manual methods of viewing and analysis, the system combines proprietary, color-based imaging technology with automated microscopy and commercially available stains and reagents.

Researchers at Sugen will use multiple ACIS capabilities, including tissue microarray analysis for research and development for tumor angiogenesis and tumor cell proliferation, the company said.

In a related development, **Xenogen Corp**. of Alameda, CA, said it has entered into a commercial licensing agreement with Sugen, involving real-time in vivo imaging technology for pre-clinical drug development studies.

The technology represents a novel approach to the biological assessment of new chemical entities, he company said. The advantages include providing higher quality data at earlier time points, resulting in a better selection of drug development candidates and significant time and cost savings, the company said.

The patented real-time in vivo imaging technology detects fluorescent or bioluminescent cells inside intact living animals, allowing non-invasive visualization and tracking of the cells to monitor the effects of treatment with NCEs, the company said. The technology also provides researchers with a way to localize and follow the expression of selected genes in vivo in the Xenogen LPTATM light-producing transgenic animals.

The technology provides improved, more predictive data and thus a better selection process for drug development candidates, the company said.

* * *

Delcath Systems Inc. (Nasdaq: DCTHU) of Greenwich, CT said NCI has approved a clinical study protocol for administering escalating dose melphalan through the Delcath drug delivery system for unresectable liver cancer.

The NCI-sponsored study would determine the maximally tolerated dose of melphalan administered via isolated perfusion through the Delcath system, the company said.

The system allows high doses of drug to be infused directly into the liver along with the organ's normal blood supply. The procedure is non- surgical and does not interrupt the natural circulation of blood within the patient, the company said. The treatment is repeatable.

The most recent studies by NCI with isolated liver perfusion techniques have involved 6-7 hour surgical procedure in which the right and left lobes of the liver are severed from their diaphragmatic attachments and various tubes and clamps are installed as part of a complex procedure to achieve complete vascular isolation of the organ, thus limiting systemic absorption of the anticancer drug, the company said. The mean hospital stay for this surgery is reported to be 11 days.

By contrast, the Delcath system is designed to achieve vascular isolation of the organ in an outpatient setting with a minimally invasive, non-surgical procedure, the company said. The system removes the majority of the drug from the blood through a sophisticated catheterization and filtration process.

At the request of the NCI, Delcath showed its system removes 99.9 percent of melphalan from blood in a laboratory setting, the company said.

Up to 27 patients will be treated under the NCI's dose-escalating protocol, the company said. A group of three patients will be treated at 60 mg/square meter of melphalan, the lowest study dose, and up to four additional groups of three patients could each receive 90, 110, 130 and 150 mg/square meter until clinicians observe unallowable toxicity and thereby establish the maximum safe tolerated dose.

"Many patients with unresectable liver malignancies are not ideal candidates for isolated perfusion with conventional surgical methods, " said H. Richard Alexander, of the NCI Surgery Branch. "Some patients are ruled out because the size or location of the tumor makes mobilization and cannulation of the liver impossible. Others have co-existent medical conditions that make the surgery an unacceptable risk. Still others who might benefit from a second procedure are no longer treatable with surgical perfusion due to the extensive scar tissue that develops around the liver after the initial procedure."

"Our hope is that the Delcath system will

provide a far less invasive way to administer high dose melphalan perfusion therapy, expanding the treatment options for patients with inoperable, life-limiting cancer of the liver," said Alexander.

* * *

Impath Inc. (Nasdaq: IMPH) said its Predictive Oncology division has signed a three-year agreement with the **University of Pennsylvania Cancer Center** for the Impath GeneBank program for the University of Pennsylvania Cancer Network, which includes 28 community hospitals.

"Through the use of unique translational genomics resources, our Impath Predictive Oncology division helps accelerate the discovery and development process for new oncology therapeutics," said Anu Saad, chairman and CEO of Impath.

The GeneBank program is an integral component of these efforts through which samples can be transformed into information for efficient, gene-based target validation and candidate selection."

* * *

Protein Design Labs Inc. (Nasdaq: PDLI) (PDL) of Fremont, CA, and **Exelixis Inc.** (Nasdaq: EXEL) (Exelixis) of South San Francisco, said they would collaborate to discover and develop humanized antibodies for the diagnosis, prevention and treatment of cancer.

The Exelixis model organism genetics technology will be used to identify new cancer drug targets; the PDL antibody and clinical development expertise will be used to create and develop new antibody drug candidates, the company said. PDL will provide Exelixis with $4 million in annual research funding for two or more years, and has purchased a $30 million note convertible after the first year of the collaboration into shares of Exelixis common stock, the companies said.

Under the agreement, PDL will receive an exclusive, worldwide license to develop antibodies against certain targets identified by Exelixis that are involved in cell growth, apoptosis and proliferation, the companies said. Exelixis will have the right to co-fund and co-develop antibodies resulting from the collaboration. For antibody products developed by PDL that Exelixis elects not to co-develop, Exelixis will be entitled to specified milestone payments and royalty payments on any product sales, the companies said.

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Tyco International Ltd. (NYSE:TYC; LSE: TYI; BSE: TYC) of Pembroke, Bermuda, a manufacturing and service company, said it would acquire **C. R. Bard Inc.** (NYSE:BCR) of Murray Hill, NJ, a multinational developer, manufacturer and marketer of health care products.

The transaction is valued at $3.2 billion, including the assumption of net debt, the company said. Bard, which had full year 2000 revenues of $1.1 billion, manufactures products used for vascular, urological and oncological diagnosis and intervention, as well as surgical specialties.

The acquisition will provide Tyco Healthcare with a new product pipeline, including new hernia repair, GERD treatment, prostate cancer and peripheral vascular disease products, as well as platforms for future acquisitions and distribution agreements, the company said.

The boards of directors of both companies have approved the transaction, which is expected to be tax-free to shareholders of C. R. Bard, the company said. Under the terms of the agreement, Bard shareholders will receive Tyco stock equivalent to $60 for each share of Bard.

* * *

Viragen Inc. (Amex: VRA) of Plantation, FL, said it has begun pre-clinical studies in collaboration with **NIH** to evaluate a monoclonal antibody for the treatment of many cancers including breast, cervical and lung.

NIH granted Viragen the exclusive worldwide commercial rights to the use of a monoclonal antibody that recognizes Notch-1 protein, the company said.

Notch-1 can regulate apoptosis, the company said. However in certain tumor cells, this process is interrupted by the over-expression of Notch 1.

"NIH have already demonstrated this effect in vitro and we are actively taking those results forward while working very closely with the NIH scientists who developed the patented technology," said Magnus Nicolson, COO of Viragen.

* * *

Xenerex Biosciences, a subsidiary of **Avanir Pharmaceuticals** (Amex: AVN) of San Francisco, and **Peregrine Pharmaceuticals Inc**. (Nasdaq: PPHM) said they have entered into an antibody research collaboration for solid tumors.

Terms of the agreement provide for the transfer of three antigen targets from Peregrine to Xenerex for the generation of fully human monoclonal antibodies, utilizing the Xenerex antibody generation technology, the companies said. Xenerex said it would receive upfront research fees and milestones and

royalties on future product sales. Peregrine said it would be responsible for product development, manufacturing and commercialization of any products developed through the collaboration.

The specific financial terms of the agreement were not disclosed, the companies said.

"Based on data from our animal models, the antibodies have the potential to be used as unconjugated antibodies for the treatment of a variety of different solid tumors," said Steven King, vice president of technology and product development of Peregrine.

Oncology Management:

NCI Selects InDex Service For Pediatric Oncology Study

(Continued from page 1)

and offsite digital imaging storage and archiving services, said NCI has selected its InDex service as its image distribution and storage provider for a national pediatric oncology study.

The service will store and distribute MRI studies as part of a clinical trial, which will be coordinated by the NCI Pediatric Oncology Branch with 10 participating U.S. pediatric hospitals, including Johns Hopkins Oncology Center of Baltimore; Children's Hospital of Philadelphia; Health Science Center of Syracuse; Texas Children's Hospital of Houston; The Children's Hospital/Dana Farber Cancer Institute of Boston; Children's National Medical Center of Washington, DC; St. Louis Children's Hospital; Children's Hospital of Los Angeles; Children's Hospital of Pittsburgh; and Children's Memorial Hospital of Chicago, the company said.

"Our InDex service will enable the study to get up and running by eliminating the need to build separate links between each facility and NCI," said Paul Dandrow, vice president of business development at InSiteOne.

"POB had some very specific requirements for the application, including secure, fast transmission from a centrally accessible, permanent archive of the studies," said Brigitte Widemann at the NCI Pediatric Oncology Branch.

The service gives NCI a faster, more flexible way to implement a digital radiological image archive because it eliminates the equipment, maintenance, technical upgrades and staffing support costs, the company said.

Clinical Trials:

Celgene Begins Two Studies With Hoffmann-La Roche

Celgene Corp. (Nasdaq: CELG) of Warren, NJ, said it has initiated two clinical studies with **Hoffmann-La Roche Inc**. of Nutley, NJ, to evaluate Thalomid (thalidomide) in combination with Xeloda (capecitabine) for colorectal cancer.

Xeloda, the first oral chemotherapy for colorectal cancer, is indicated as first-line treatment for metastatic colorectal cancer when treatment with fluoropyrimidine therapy alone is preferred, the company said.

Combination chemotherapy has shown a survival benefit compared to 5-FU/LV alone; a survival benefit has not been demonstrated with Xeloda monotherapy as with the combination chemotherapy, the company said. Use of Xeloda instead of 5-FU/LV combinations has not been adequately studied to assure safety or preservation of the survival advantage.

Celgene will also support a 20-patient pilot trial at Baylor College of Medicine at the Texas Medical Center evaluating the safety and efficacy of Interferon-alpha with Xeloda and Thalomid for metastatic renal cell carcinoma.

"We intend to evaluate the potential of these two oral agents as a combination therapy with a well-tolerated dose of Interferon-alpha," said Robert Amato, lead trial investigator at Baylor College of Medicine.

Thalomid was approved in 1998 for cutaneous manifestations of moderate to severe erythema nodosum leprosum and as maintenance therapy for prevention and suppression of cutaneous manifestation recurrences, the company said.

* * *

Antisoma plc of London, said it would extend recruitment to the phase III SMART study of pemtumomab (formerly known as Theragyn) for ovarian cancer.

The SMART study is designed to determine whether Yttrium-90 radiolabelled pemtumomab, in addition to current standard care, demonstrates a benefit over standard care alone, the company said.

The company was advised by FDA that the level of statistical significance of the data should be increased to $p<0.01$ from the original study design of $p><0.05$, the company said. As a result, the total number of events has risen from 80 to 116. An additional number of patients will be recruited to achieve the new end

point, the company said. The projected date of filing for marketing approval will be unlikely before 2004, the company said.

* * *

British Biotech (LSE: BBG; Nasdaq: BBIOY) of Cambridge, MA, and **ImmunoGen Inc**. (Nasdaq: IMGN) said they have begun enrollment for a phase I/II study to evaluate the safety, pharmacokinetic profile and biological activity of the tumor-activated prodrug, BB-10901/huN901-DM1, for small cell lung cancer.

BB-10901 was created by conjugating the chemotherapeutic agent, DM1, a maytansinoid, with the humanized monoclonal antibody, huN901, which binds to a protein found on the surface of SCLC cells, the company said.

The first phase of the open-label, dose-ranging study will evaluate the safety and maximum tolerated dose of the drug. In the phase II part, 80 patients will receive a once-weekly, intravenous dose of BB-10901 for four weeks, followed by two weeks off. Treatment cycles can be repeated.

The study is being conducted by Frank Fossella, at M.D. Anderson Cancer Center, and Anthony Tolcher, at the Institute for Drug Development of the Cancer Therapy and Research Center in San Antonio.

* * *

Matritech Inc. (Nasdaq: NMPS) of Newton, MA, said it has initiated the investigation of its NMP66 breast cancer screening blood test in Germany, a parallel trial to a multi-center clinical study in the U.S.

The investigators in Germany are: Rolf Kreienberg, director of the Department of Obstetrics and Gynecology of the University of Ulm and president of the German Cancer Society; Katarzyna Michniewicz of the Frauenklinik, Department of Obstetrics and Gynecology at the Oskar Ziethen Krankenhaus, Humboldt University in Berlin; Diana Lueftner, Department of Oncology and Hematology, Charite Hospital, Humboldt University, coordinator of the Breast Cancer Biochemical Marker Study Group at the Charite, member of the Matritech Breast Cancer Medical Advisory Board and coordinator of the NMP66 research.

The studies are intended to evaluate the ability of NMP66 to detect breast cancer, differentiate between benign and malignant lesions, and identify patients with normal mammograms, the company said.

Detection of the breast cancer markers in blood was accomplished using mass spectrometry, the company said. In addition to the mass spectrometry format, the company said it is pursuing antibody-based immunoassays compatible with existing clinical laboratory instrumentation.

The Matritech nuclear matrix protein core technology correlates levels of NMPs in body fluids to the presence of cancer, the company said. A pipeline of NMP-based products is in development for the detection of major cancers including cervical, breast, colon and prostate cancers, the company said.

The NMP22 Test Kit for bladder cancer is cleared for marketing in the U.S. for management and screening of individuals at risk of bladder cancer, the company said. It also is sold in China, Europe and Japan where it is approved for bladder cancer screening.

* * *

MetaPhore Pharmaceuticals Inc. of St Louis said it has received FDA investigational new drug application approval to begin phase I trials of M40403 for advanced skin and end-stage kidney cancers.

The study will test the safety and tolerability and pharmacokinetics in normal, healthy subjects, as a precursor to phase II trials in which the compound will be tested in conjunction with interleukin-2, the company said.

M40403 is a proprietary family of enzyme mimetic compounds that mimic the action of one of the primary free-radical fighting mechanisms of the body, the natural enzyme superoxide dismutase, the company said.

Preclinical studies at the Huntsman Cancer Institute in Salt Lake City have shown that M40403 improves the effectiveness of IL-2, an approved treatment for inoperable metastatic melanoma and metastatic renal-cell carcinoma, the company said. "The SOD enzyme mimetic may offer improved therapeutic options for end-stage cancer patients, with a greatly reduced side-effect profile," said Wolfram Samlowski, a MetaPhore principal collaborator with the Huntsman Cancer Institute.

The natural SOD enzyme plays a central role oxidative chemistry, regulating normal levels of free-radical superoxide molecules, the company said. In certain disease states, however, the immune system prompts an overproduction of superoxide free radicals and the natural SOD enzymes become overwhelmed, leading to tissue and cell damage.

Free radicals also play a role in the natural blood-pressure regulatory system. In excess, superoxide free radicals deactivate a class of molecules, catecholomines that constrict blood vessels, resulting

in hypotension, the company said. By reducing the level of superoxide, the SOD enzyme mimetics have been shown to reverse hypotension and effectively restore blood pressure in several different animal models. The studies formed the basis for the exploration of enzyme mimetics as a co-therapy with IL-2 cancer treatment.

* * *

MediGene AG (NMarkt: MDG) of Planegg, Germany, announced the start of a phase I/II trial for a vaccine against malignant melanoma developed together with Aventis Pharma AG. The therapeutic vaccination is based on gene transfer by so-called adeno-associated viruses (AAV).

For the achievement of this milestone MediGene received a payment of DM 2 million from Aventis Pharma.

The first step of the therapy against malignant melanoma is the excision of the tumor. For the production of the vaccine immune activating genes are then introduced into these tumor cells in the laboratory, the company said. This gene transfer is performed using non-pathogenic adeno-associated viruses. After a treatment that stops further growth of the tumor cells the modified cells are administered to the patient.

The study will be performed in several European countries and will include stage IV patients whose disease progressed on immune therapy and chemotherapy. Under the agreement, MediGene is responsible for the development of the AAV-technology. The two companies will collaborate on phase 1 and phase 2 trials, but Aventis will be responsible for the phase III trials, registration and marketing.

* * *

EntreMed Inc. (Nasdaq: ENMD) of Rockville, MD, and Aventis Pharmaceuticals said they will collaborate on phase II trials of daily oral Panzem in combination with weekly Taxotere (docetaxel) for prostate hormone-refractory prostate cancer. Endpoints will include tolerability, PSA levels, and tumor response, the companies said.

Panzem (2-methoxyestradiol (2ME2)) is a naturally occurring molecule that, in preclinical models, has inhibited tumor growth as well as the growth of blood vessels, the companies said. Its oral dosing formulation, the agent is evaluated in

Panzem, the fourth angiogenesis inhibitor brought to the clinic by EntreMed, is the company's first product candidate that has been shown in preclinical testing to attack both compartments of cancer: tumor cells and their blood supply, the company said.

* * *

Vion Pharmaceuticals Inc. (Nasdaq: VION) of New Haven, CN, has initiated a phase I trial of Sulfonyl Hydrazine Prodrug (SHP) VNP40101M, an anticancer alkylating agent that has demonstrated broad anti-tumor activity in preclinical studies.

The multi-center study is being conducted at the West Haven Veterans Administration Hospital in Connecticut, the Yale Cancer Center in New Haven and the Arizona Clinical Research Center in Tucson, the company said.

VNP40101M inhibits a key enzyme (AGT) involved in the repair of the DNA damage, making it more difficult for cancer cells to develop resistance, the company said. According to the company, the agent had demonstrated an ability to cross the blood-brain barrier.

"VNP40101M is Vion's third anticancer agent and our first clinical candidate from the SHP class of novel alkylating agents," said Mario Sznol, Vion's vice president, clinical development. "Alkylating agents have proven efficacy in the treatment of certain types of cancers, and the preclinical data suggest that VNP40101M has distinct advantages over existing agents and therefore may eventually lead to improved treatment for some patients."

Product Approvals & Applications:

FDA Approves Manufacturer Of IVAX Paclitaxel Ingredient

IVAX Corp. (AMEX:IVX) of Miami, said FDA has approved an additional manufacturer of the paclitaxel active ingredient and an additional manufacturer of finished product for its paclitaxel injection product.

IVAX has been marketing generic paclitaxel in the U.S. since October 2000, and has sold $120 million of the product.

"The demand for our brand equivalent paclitaxel product has been very strong, and these approvals will permit us to supply a significantly greater part of the market," said Neil Flanzraich, vice chairman and president of IVAX.

The company said it has received patent approval for formulations and methods allowing the administration of orally therapeutic agents such as paclitaxel and other agents that are normally

administered by injection or infusion.

* * *

EDG Capital Inc. (OTCBB: EDGN) of Garden City, NY, a developer of nuclear oncology pharmaceuticals, said its subsidiary **Isotope Solutions Inc**. filed an investigational new drug application with FDA to test its radioactive cisplatin technology for liver cancer.

Medical research groups managed by ISI will be conducting the testing, the company said.

The radioactive cisplatin, 195mPt-Cisplatin, is chemically identical to standard cisplatin except that the platinum it contains has been made radioactive, the company said. Cisplatin binds with tumor cell DNA, thereby disrupting its reproduction. Radioactive cisplatin is designed to deliver high doses of radioactivity directly into the tumor cells.

"Radioactive cisplatin represents the next step forward in the platinum-based treatment of cancers," said Jack Schwartzberg, president, chairman and CEO of EDG Capital. "Our radioactive cisplatin may find future application in the treatment of many types of cancers, including liver, bladder, lung, brain, gastric, head and neck, pancreatic, esophageal, gynecological, breast, colon and prostate."

* * *

Guilford Pharmaceuticals Inc. (Nasdaq: GLFD) of Baltimore said FDA has accepted for priority review its supplemental new drug application to expand the labeled indication for Gliadel Wafer (polifeprosan 20 with carmustine implant) to include first line therapy for newly diagnosed malignant glioma.

The first new therapy to be approved for the treatment of brain cancer in over two decades, Gliadel Wafer received marketing approval from FDA in September 1996 for glioblastoma multiforme, the company said. It is approved for use for recurrent surgery in 21 countries worldwide.

The therapy is a small, white dime-sized wafer made of a biodegradable polymer that contains the cancer chemotherapeutic drug, carmustine or BCNU, the company said. Up to eight wafers can be implanted in the cavity created when a brain tumor is surgically removed. The wafers slowly dissolve over a period of 2 to 3 weeks, delivering chemotherapy directly to the tumor site in high concentrations, while minimizing drug exposure to other areas.

"The therapy is approved to treat only the 30 percent of patients who experience tumor recurrence," said Craig Smith, president and CEO of Guilford. However, should Gliadel Wafer receive approval from the FDA for use at the time of initial diagnosis and surgery, we're hopeful that we can bring the treatment benefits of localized chemotherapy with Gliadel Wafer to more patients worldwide."

Gliadel Wafers have been well tolerated, the company said. They contain carmustine and should not be given to patients who are allergic to carmustine.

* * *

Intuitive Surgical Inc. of Mountain View, CA, a surgical robotics company, said it has received market clearance from FDA to expand its da Vinci Surgical System and endoscopic instruments for performance of laparoscopic radical prostatectomy.

The surgical system allows surgeons to perform the procedure through minimally invasive surgical incisions, reducing pain, blood loss, and recovery time, the company said.

The da Vinci Surgical System, the only robotic system that has received market clearance by FDA to perform surgery, consists of a control console with integrated, high-performance InSite 3-D vision system for viewing, a patient-side cart of three robotic arms that position and precisely maneuver endoscopic instruments and an endoscope, and a variety of articulating EndoWrist Instruments, the company said.

* * *

R2 Technology of Los Altos, CA, said FDA has expanded approval for its ImageChecker CAD system, a computer aided detection technology for breast cancer, to include diagnostic mammograms.

The technology can improve breast cancer detection with screening mammography by up to 20.5 percent, the company said. The ImageChecker, approved in 1998 for use with screening mammography, helps radiologists minimize false negative readings during mammograms, the company said.

* * *

Draxis Health Inc. (Nasdaq: DRAX)(TSE:DAX.) of Missisauga, Ontario, said its radiopharmaceutical subsidiary, Draximage Inc., has received FDA approval to market palladium-103 brachytherapy implant (BrachySeed Pd-103) for the treatment of prostate cancer and other selected localized tumors, including tumors of the head, neck, lung, pancreas, breast, and uterus.

Palladium-based brachytherapy implants account for about 40% of the U.S market, and are predominantly used with more aggressive tumors. Earlier this year, the company began another product, BrachySeed I-125 in Canada and the U.S.

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