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Oncology Practice Group Leaves Allegheny For Former Rival UPCI; Will NSABP Follow?

The University of Pittsburgh Cancer Institute has absorbed its only formidable competitor, Oncology Hematology Associates of Western Pennsylvania.

This is no small catch for Pitt. OHA's oncologists see 12,000 new patients a year, about 2,000 patients more than Pitt, an NCI-designated comprehensive cancer center.

What's more important, OHA was affiliated with Pitt's cross-town rival, the financially troubled Allegheny General Hospital. In fact, all of Allegheny General's oncology was handled by the practice.

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In Brief:

Cornell, MSKCC, Rockefeller To Collaborate In $160M Basic Biological Research Program

THREE NEW YORK INSTITUTIONS have formed a $160 million collaborative program in basic biological research as a result of a donation of half the funding by an anonymous donor. The collaboration among Cornell University and its Weill Medical College, Memorial Sloan-Kettering Cancer Center, and Rockefeller University will include the joint recruitment of a dozen new faculty members over the next five to 10 years, the institutions said in announcing the joint venture on June 27. "This new and unique institutional collaboration of these outstanding research centers will allow us to take on the most exciting intellectual challenges of the 21st century: how to utilize the full knowledge of the human genome and how to apply new technologies in structural biology and nanotechnology to advance human health," said **Hunter Rawlings**, president of Cornell. The joint faculty appointees will have full privileges at each of the institutions. Visiting investigator programs and enhanced telecommunications links are planned to facilitate collaborator among investigators based in Ithaca and Manhattan. Plans are being developed for a shared graduate program. The partnership plans to form core facilities for fundamental technologies such as high-performance computing, physical analysis of molecular structure, light and electron microscopy, DNA sequencing and other tools for genetic analysis, and the broad range of chemical techniques that are applied to biology. The partnership will be governed by the leaders of each institution. "The technological requirements for fully utilizing our new understanding of the human genome extend beyond the discipline of biology and the boundaries of any single institution,"

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With Stronger Accrual, UPCI May Try To Lure Back NSABP

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The practice also was one of the top contributors of patients for clinical trials of the National Surgical Adjuvant Breast & Bowel Project, the cooperative group based at Allegheny General.

Pitt officials say that, after the merger, the cancer center will be able to combine UPCI's basic science and a formidable capacity to accrue patients. Several insiders said Pitt may now be in a better position to lure back NSABP, which left for Allegheny in 1997.

The cooperative group left in the midst of a nationally publicized controversy that began with admission of scientific fraud by a Montreal investigator, led to Chairman Bernard Fisher's dismissal by then NCI Director Samuel Broder, and culminated in Fisher's suit against Pitt.

Now, NSABP is controlled by the NSABP Foundation, which means that the group will be able to move to another institution with relative ease. Sources at NSABP said the group is negotiating with several institutions inside and outside the state.

The cooperative group's current chairman Norman Wolmark left Pitt four years earlier, as a result of an unrelated dispute with Pitt officials. Since that time, the Pitt administration has changed, as Thomas Detre, the official who figured in both disputes, retired from his post as senior vice chancellor for health sciences.

Negotiations Began With Allegheny Bankruptcy

The negotiations between Pitt and OHA began about a year ago, when Allegheny General's parent entity, Allegheny Health, Education, Research Foundation, went into bankruptcy.

The deal, which involves no up-front cash, will make OHA oncologists employees of the university, officials said.

"I think this approach provides a new opportunity to bring community oncologists together with academic clinical oncology," Ronald Herberman, director of UPCI and the University of Pittsburgh associate vice chancellor for health sciences research, said to **The Cancer Letter**. "They are being brought in completely into the cancer institute and the University of Pittsburgh Medical Center."

Altogether, three health systems were vying for the practice, said OHA President Stanley Marks, who founded the practice in 1978. The practice chose Pitt, because it offered the potential of creating one of the premier cancer centers in the country.

"This was the most attractive proposal from the long-term growth and security potential," said Marks, who has assumed the additional position of deputy director for medical oncology for UPCI.

"There is a potential because of the volume of patients coming through, as well as the UPCI research," Marks said to **The Cancer Letter**. "Combining a huge patient base with a tremendous research organization could make us competitive with the top cancer centers."

OHA employs 30 oncologists who work in 21 locations. UPCI employs 27 faculty members at the University of Pittsburgh School of Medicine and 18 community physicians who are medical oncologists. Marks said OHA saw 12,000 new patients last year, and PCI saw 10,000.

The headquarters of the UPCI research and clinical activities will be based in the Hillman Cancer Center, on the UPMC Shadyside campus in Pittsburgh. The building is scheduled to open in the summer of 2002.

Jeffrey Shogan, co-managing partner of OHA, will become associate deputy director of clinical oncology at UPCI. Shalom Kalnicki, a radiation oncologist associated with OHA, will become vice chairman of radiation oncology for UPCI as a result of this transaction. Donald (Skip) Trump, will continue

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Founded Dec. 21, 1973, by Jerry D. Boyd

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as deputy director for clinical investigations at UPCI and will have the central responsibility for clinical and translational research.

Until the Hillman Cancer Center is completed, most oncology treatment would be offered through the current outpatient sites of the OHA and UPCI.

"For UPCI, the importance of a strong network of community physicians cannot be overestimated," said Arthur Levine, senior vice chancellor for health sciences and dean of the Pitt School of Medicine. "This component is necessary for clinical research to flourish and to insure that the largest number of patients has access to new treatments as soon as they become available."

OHA is managed by US Oncology Network. The merger will expand the availability of trials at Pitt. "We have trials that are different from their trials; they have trials that are different from ours, and together we participate in Eastern Cooperative Oncology Group and NSABP," said Marks.

UPCI said it is negotiating with US Oncology to manage all of its community specialty practices and explore the development of regional cancer centers.

Human Genome Consortium Completes "Working Draft"

The Human Genome Project public consortium said June 26 that it has assembled a working draft of the sequence of the human genome.

The milestone involved two tasks: placing large fragments of DNA in the proper order to cover all of the human chromosomes, and determining the DNA sequence of these fragments.

The assembly consists of overlapping fragments covering 97 percent of the human genome, of which sequence has already been assembled for approximately 85 percent of the genome.

More than 60 percent of the sequence was produced in the past six months. During this time, the consortium has been producing 1000 bases a second of raw sequence, seven days a week, 24 hours a day.

The average quality of the "working draft" sequence far exceeds the consortium's original expectations for this intermediate product, officials said.

Consortium centers have produced far more sequence data than expected (over 22.1 billion bases of raw sequence data, comprising overlapping fragments totaling 3.9 billion bases and providing 7-fold sequence coverage of the human genome).

As a result, the "working draft" is substantially closer to the ultimate "finished" form than the consortium expected at this stage. Approximately 50 percent of the genome sequence is in near-finished form or better, and 24 percent of it is in completely "finished" form. Across the genome, the average DNA segment resides in a continuous gapless sequence "contig" of 200,000 bases. The average accuracy of all of the DNA sequence in this assembly is 99.9 percent.

The sequence information from the public project has been publicly released. Already, many tens of thousands of genes have been identified from the genome sequence. Analysis of the current sequence shows 38,000 predicted genes confirmed by experimental evidence. There are many thousands of additional gene predictions to be tested experimentally. Dozens of disease genes have been pinpointed by access to the working draft.

The consortium's goal for the spring of 2000 was to produce a "working draft" version of the human sequence, an assembly containing overlapping fragments that cover approximately 90 percent of the genome and that are sequenced in "working draft" form, with some gaps and ambiguities.

The consortium's ultimate goal is to produce a completely "finished" sequence, with no gaps and 99.99 percent accuracy.

In a related announcement, Celera Genomics, of Rockville, MD, announced that it has completed its own first assembly of the human genome DNA sequence.

The public and private projects use similar automation and sequencing technology, but different approaches to sequencing the human genome. The public project uses a "hierarchical shotgun" approach in which individual large DNA fragments of known position are subjected to shotgun sequencing (shredded into small fragments that are sequenced, and then reassembled on the basis of sequence overlaps).

The Celera project uses a "whole genome shotgun" approach, in which the entire genome is shredded into small fragments that are sequenced and put back together on the basis of sequence overlaps.

The hierarchical shotgun method has the advantage that the global location of each individual sequence is known with certainty, but it requires constructing a map of large fragments covering the genome. The whole shotgun method does not require

this step, but presents other challenges in the assembly phase. Both approaches align the sequence along the human chromosomes by using landmarks contained in the physical map produced by the Human Genome Project.

"The two approaches are quite complementary. The public project and Celera plan to discuss the relative scientific merits of the methods employed by the two projects. In the end, the best approach may well be to use a combination of the methods for sequencing future genomes," said Francis Collins, director of the National Human Genome Research Institute. Current plans by the public project to sequence the genome of the laboratory mouse involve this hybrid strategy.

The Human Genome Project will now focus on converting the "working draft" and near-"finished" sequences to a "finished" form, officials said. This will be done by filling the gaps in the "working draft" sequence and by increasing the overall sequence accuracy to 99.99 percent. Although the "working draft" version is useful for most biomedical research, a highly accurate sequence that is as close to perfect as possible is critical for obtaining all the information there is to get from human sequence data. This has already been achieved for chromosomes 21 and 22, as well as for 24 percent of the entire genome.

The greater-than-expected sequence production has also yielded a bumper crop of human genetic variations, called single nucleotide polymorphisms or SNPs. The Human Genome Project had set a goal of discovering 100,000 SNPs by 2003. Already, with the assembled sequences and other data accumulated by The SNP Consortium, scientists have now found more than 300,000 SNPs and will likely have 1 million SNPs by year-end. These SNPs provide a powerful tool for studies of human disease and human history.

The international Human Genome Sequencing consortium includes scientists at 16 institutions in France, Germany, Japan, China, Great Britain and the United States. The five largest centers are Baylor College of Medicine, Houston; Joint Genome Institute, Walnut Creek, CA; Sanger Centre near Cambridge, England; Washington University School of Medicine, St. Louis; and Whitehead Institute, Cambridge, MA. Together, these five centers have generated about 82% of the sequence.

The project is funded by grants from government agencies and public charities, including the National Human Genome Research Institute at the National Institutes of Health, the Wellcome Trust in England, and the U.S. Department of Energy.

The total cost for the working draft is approximately $300 million worldwide, with roughly half ($150 million) being funded by NIH. The cost of sequencing the human genome is sometimes reported as $3 billion. However, this figure refers to the original estimate of total funding for the Human Genome Project over a 15-year period (1990-2005) for a wide range of scientific activities related to genomics. These include studies of human diseases, experimental organisms (such as bacteria, yeast, worms, flies and mice), development of new technologies for biological and medical research, computational methods to analyze genomes, and ethical, legal and social issues related to genetics.

NCI Programs:

Institute Plans $40M In Grants For Cancer Outcomes Studies

The NCI Board of Scientific Advisors last week approved the Institute's plan to set aside $40 million over the next five years to fund a consortium of grantees to study outcomes and quality of life in cancer care.

The new program represents a major step by the Institute to begin developing ways to measure and improve the quality of cancer care, and complements work underway by the American Society of Clinical Oncology and the National Cancer Policy Board to study the issue of quality of cancer care, said Barbara Rimer, director of the NCI Division of Cancer Control and Population Sciences.

The concept for the program, called Cancer Care Outcomes and Surveillance Consortium, or CanCORS, was presented to the BSA last March, but tabled after board members criticized it for a lack of focus and questioned the project's feasibility. A subcommittee of the board worked with NCI staff to rewrite the concept statement. The new version is more streamlined and will begin by studying outcomes in two diseases, breast and colorectal cancer, NCI officials said.

BSA member Suzanne Fletcher, of Harvard Pilgrim Health Care, said the consortium would fill a gap in academic research. "The need to understand what is happening out there in the community is crucial," she said. "We don't know why what we're getting is not reflected in the SEER data. The side effect of this is to get academic cancer center people working with population-based groups,"

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Some BSA members questioned the consortium model of the program. "What's missing is hypothesis driven research," said David Alberts, director of cancer prevention and control at the Arizona Cancer Center. "I'm concerned about open-ended research."

"Why not put the goals out there and let people respond with how we're going to achieve the goals?" said Richard Schilsky, associate dean for clinical research, University of Chicago.

NCI's Rimer said the Institute has supported too many outcomes studies that can't be compared. "There is always a tension between a cooperative approach and an individual approach," she said. "I think the process will end up with the kind of group you are suggesting, but without the perils of the other approach, where you end up with a lot of people using disparate approaches.

"As we've looked at our studies, you can't compare many of them.," Rimer said. "You can't compare studies even in mammography, because each investigator has a different way of asking the question. This really is a cooperative approach, enabling the research."

BSA member David Abrams, director of the Center for Behavioral and Preventive Medicine at Brown University School of Medicine, noted that a panel advising NCI on its cancer control program strongly recommended this type of research program.

The BSA approved the concept on a vote of 18-1, with four abstentions.

Following are excerpts of the concept statement:

Cancer Care Outcomes and Surveillance Consortium (CanCORS). Concept for a new RFA, five to 14 cooperative agreement awards for five years, first-year set-aside $6 million, total cost $40 million. Program director: Arnold Potosky, DCCPS, phone 301-496-8500, email ap40g@nih.gov.

The goals of CanCORS address three major new priorities at NCI:

1. Enhance monitoring and understanding of the processes of cancer care and patient-centered factors influencing prognosis in population-based cohorts of patients.

2. Establish a system for examining the relationship of the processes of care to clinical and patient-centered outcomes, with emphasis on measuring the dissemination of state-of-the-science interventions and their association with better quality outcomes in the general population of cancer patients.

3. Examine disparities in the receipt of state-of-the-science cancer care and factors that contribute to disparities in outcomes (such as health-related quality of life) and identify ways to lessen those disparities.

This is the first major step by NCI to develop a system for obtaining details about cancer care beyond the initial surgical and radiation treatment that is now routinely collected in high quality cancer registries. This will complement the SEER Program and other population-based cancer registries and build the information base needed for measuring and improving the quality of cancer care in the U.S.

Support will be provided to conduct large, prospective cohort studies of patients with newly diagnosed lung, colorectal, breast, and prostate cancer. A new infrastructure will be formed to support between 5-7 research teams for each site, though research teams may participate in multiple cancer sites. The research goal will be accomplished with two separate but closely related RFAs, starting with a RFA focusing on lung and colorectal cancers issued in the summer of 2000, followed by a breast and prostate cancer RFA issued in spring 2001. Each research team will collect data within large, well-defined populations and provide core data to a central statistical coordinating center to ensure standardization and enable pooled analyses. The participation of high-quality population-based cancer registries is particularly encouraged.

In the initial RFA described by this concept, there will be a target sample of 5,000-7,000 newly diagnosed lung and the same number of newly diagnosed colorectal cancer patients enrolled within 4-6 months after initial treatment. Core data on processes and outcomes of care for all enrolled patients will be collected by all participating institutions using multiple sources (inpatient and outpatient medical records, patient surveys, administrative data). Information on other potential prognostic factors such as smoking history, use of nonsteroidal anti-inflammatories, weight, diet, or physical activity may also be collected. In addition to core data and primary research objectives, research proposals will be invited to conduct studies in selected samples of patients to focus on specific questions complementing the core study; for example, surveys of providers to assess reasons for observed practice patterns, more detailed evaluation of the clinical decision making process, the use of alternative therapies, or specific studies examining the role of established prognostic biomarkers among defined patient subgroups. The

study cohort will be dynamic in that new patients can be added in subsequent years in order to track newly emerging technologies.

Total cost per each cancer (lung and colorectal) is $20 million over a five-year period, including the budget for the statistical coordinating center (SCC). This estimate is based on assumptions of approximately $1,700-$2,200 in direct costs per patient enrolled, estimated enrollment of 6,000 cases, 15-20% of direct costs for special research projects, and indirect costs of approximately 50%. The estimate for the SCC for covering the lung and colorectal research effort is $500,000 to $600,000 per year over five years. Total cost over five years of the RFA is approximately $40 million, and $6 million in year 1. The four succeeding years will be funded at approximately $8.5 million per year because of increasing resources required for enrollment and data collection. Assuming a continued need to examine the long term processes and outcomes of cancer care, we anticipate a need for a competitive renewal at five years in order to extend follow-up of the original cohort, or to enroll new cohorts.

Other Concept Approvals

Other concept statements approved by the BSA at its June 22 meeting follow:

Innovative Cancer Complementary and Alternative Medicine Initiative in Cancer Centers. Concept for a new RFA, seven P30 supplement awards for three years, first-year set-aside $2 million, total $6 million. Program director: Jeffrey White, director, Office of Cancer Complementary and Alternative Medicine, phone 301-435-7773, email jw136e@nih.gov.

There is a paucity of R01 funded research grants in the field of cancer complementary and alternative medicine. To increase the number and quality of investigator-initiated R01 research grants on cancer CAM, the NCI Office of Cancer Complementary and Alternative Medicine and the NIH National Center for Complementary and Alternative Medicine (NCCAM) propose to co-fund supplements to clinical and comprehensive P30 cancer centers. Applications will undergo competitive review by NCI. Each application will contain up to three pilot projects and each award will provide up to $300,000 in total cost.

The intent of this initiative is to encourage and support the development of basic, epidemiological, and clinical (prevention, therapeutic, and palliative) CAM cancer research within NCI-supported cancer centers. Pilot and phase I and II clinical trials may be included as projects.

Another goal of this project is to facilitate communication and collaboration between the CAM practitioner and the conventional cancer research communities. CAM covers a broad range of healing philosophies, approaches, and therapies. The classification of healthcare practices considered CAM by the NCCAM is on the Web at http://nccam.nih.gov/nccam/fcp/classify/.

Collaborations on Nutritional Modulation of Genetic Pathways Leading to Cancer. Concept for a new RFA, four to six awards, first year set-aside $1.2 million, total set-aside $45.1 million over five years. Program director: John Milner, acting chief, Nutritional Sciences Research Group, Division of Cancer Prevention, phone 301-496-0118, email milnerj@mail.nih.gov.

This RFA will create a new interdisciplinary approach to resolving issues about the physiological significance of dietary components as regulators of genetic and epigenetic pathways involved with cancer. The establishment of these large-scale collaborative projects will simultaneously create programs of excellence that will serve as models for future research programs. This strategy will embody new and innovative preclinical and clinical approaches to deciphering the role of nutrition in cancer prevention. These collaborative and integrative research programs should expedite the delineation about how specific dietary components influence genetic pathways and allow for the utilization of this information to address more complex and synthetic questions that take into account the whole organism. It is anticipated that the information gained will provide guidance for the development of dietary intervention strategies that are effective in cancer prevention.

The following are examples of some of the areas of research that are viewed as relevant for this RFA:

—Use of natural genetic variations to elucidate how nutritional exposures are linked to phenotype

—Characterization of molecular events that govern the ability of specific nutrients to alter cell cycle checkpoints

—Credentialing of target receptors for cancer prevention that are modified by dietary constituents

—Methylation patterns that are influenced by dietary manipulations that influence gene expressions and cellular phenotypes

—Antioxidant scavenging and oxygen stress modulation by nutrients

—DNA repair mechanisms influenced by dietary constituents

—Signaling pathways that regulate cancer growth, development, differentiation and apoptosis as regulated by dietary components

—Features of DNA damage, DNA repair or cell cycle progression that make them particularly susceptible to dietary intervention strategies

This RFA will be structured in two phases. Phase I, lasting about six months, will be used to allow scientists time to identify key components needed for the large collaborative project. During this formulating phase the participating scientists and resources would be identified and the overall conceptual framework defined. Phase II will be the actual large-scale collaborative project and will include benchmarks for assessing accomplishments. Each large-scale collaborative project award must include an administrative management plan. The actual organizational structure for a collaborative project may vary depending on the specific research problem. Large-scale collaborative projects may consist entirely of a research and administrative structure that facilitates data coordinating and information dissemination. A large-scale collaborative project may also include: (a) Pilot projects aimed at enriching approaches or techniques available to the large-scale project and/or adding investigators outside the scientific mainstream of the project and (b) Core resources to speed progress in the collaborative project or improve technologies.

Domestic and foreign organizations, public and private institutions are eligible. Minority institutions and investigators will be encouraged to participate.

The Collaborative Project will be developed around scientists with expertise to delineate the role that diet has in regulating genes involved with cancer. Each Collaborative Project must include expertise in nutrition and genetics. Participating members of the Collaborative Group must have external, peer-reviewed research support. These investigators may be at the same institute as the PI or at a different location. Merits of each Collaborative Project will be based on the sciences embodied to address the role of diet and genetics in cancer prevention.

Each Phase II award would be 5 years in duration. A cost adjustment of 3% per year is proposed. Appropriate reimbursement for Phase I expenses may include salary for release time for the PI to plan the Phase II application, cost associated with steering committee meetings and participating investigators, and for consultants involved with the initial design.

Technologies for Comprehensive, Quantitative Protein Analysis in Human Tumors. Concept for a new RFA, three to five awards over four years, first-year set-aside $1.5 million, total set-aside $6.5 million. Program director: Min Song, Cancer Diagnosis Program, Division of Cancer Treatment and Diagnosis, phone 301-402-4185, email ms425z@nih.gov.

The purpose of this initiative is to support the development of innovative technologies for the quantitation of the complete spectrum of proteins present in human tissues. In combination with protein identification strategies, sensitive, efficient, and reproducible protein quantitation technologies are needed to more accurately and rapidly determine altered levels of individual proteins in human tumor specimens. The approaches proposed should take into account the need to identify and quantitate a broad range of proteins including proteins present in low abundance and proteins that are membrane-associated or not readily soluble. Approaches should be sensitive enough to detect modest changes in protein concentrations since these changes may have significant biological consequences.

Investigators will be asked to develop technologies for both comprehensive identification and quantitation of proteins present in human tumor specimens. They may propose to analyze the spectrum of proteins and changes in protein expression levels. Further identification of the proteins may be achieved by linking protein data to mRNA expression databases, peptide mapping databases, three-dimensional protein structure databases, and/or protein function databases. Individual proteins may be further characterized by amino acid sequence, molecular weight, post-translational modifications, or proteolytic peptide maps. Investigators may also choose to identify and quantitate the proteins present in subcellular compartments of human tissues.

Program staff proposes to use the R21/R33 phased innovation award mechanism to support projects proposed in response to this initiative. In the R21 phase, investigators will demonstrate the feasibility of their technologies in comprehensive, quantitative analysis of proteins present in human tumor specimens. In the R33 phase, investigators will

further develop the proposed approaches into sensitive, efficient, and reproducible quantitation technologies that work in conjunction with protein identification strategies. Applicants will be able to choose one of three options in submitting proposals: an R21 proposal alone, a combined R21/R33 proposal, or an R33 proposal alone if feasibility of the project can be documented.

In Brief:

North General, MSK, Form Cancer Prevention Center

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said **Harold Varmus**, MSK president. "We recognize that New York's strength in the scientific arena depends on our ability to work together." The three areas targeted for development are chemical biology, computational biology, and cancer biology, the institutions said. . . . **RALPH LAUREN CENTER** for Cancer Prevention and Care, a collaboration between North General Hospital of New York and Memorial Sloan-Kettering Cancer Center, will offer comprehensive education, screening and diagnostic services for a range of cancers including breast, prostate, lung, cervical and colon, as well as treatment and referrals for the Harlem community. As part of its continuum of care, the center, which will be located at North General Hospital, will provide a patient navigator service that follows patients throughout their treatment helping them with the complexities of the healthcare system. The initiative, a result of a 20-year collaboration between **Harold Freeman**, president and CEO of North General and the Breast Examination Center of Harlem, a Memorial program also directed by Freeman, is made possible by a $5 million gift from the Polo Ralph Lauren Corp. "This extraordinary gift will make a difference in the lives of people who suffer disproportionately from cancer," said Freeman, recently named associate director for reducing health disparities at NCI. "I believe that this is one of the most important and exciting projects undertaken by our center," said **Harold Varmus**, president of Memorial. "Everything we have accomplished at the Breast Examination Center of Harlem has been a prologue leading us to this natural next step." . . . . **YOUR CANCER RISK**, the Harvard Center for Cancer Prevention Web site, now offers a personalized method for estimating and lowering the risk of the 12 most common cancers. The interactive risk assessment tool is different from most on-line health information because "it offers people a road map, showing them which steps have the biggest impact, given their lifestyle and background," said **Graham Colditz**, director of education at the Harvard Center for Cancer Prevention and professor of epidemiology at Harvard School of Public Health. The site: http://www.yourcancerrisk.harvard.edu . . . . **WHITE HOUSE** Office of Science and Technology Policy released a report describing its annual $80 billion federal R&D innovation expenditures investments in each of the 50 states, the District of Columbia and Puerto Rico. The report makes the case for increasing federal R&D investments by looking at evidence of its ripple effect on all levels of the economy. The report is available at http://www.whitehouse.gov/WH/EOP/OSTP/html/radius.html. . . . **STEVEN BURAKOFF**, the Margaret M. Dyson Professor of Pediatrics at Harvard Medical School, chairman of the Department of Pediatric Oncology at Dana-Farber Cancer Institute, and an expert in immunology and translational research in bone marrow transplantation, was appointed director of the Kaplan Comprehensive Cancer Center and the Laura and Isaac Perlmutter Professor and director of the Skirball Institute of Biomolecular Medicine, effective Sept. 1, by **Robert Glickman**, dean of New York School of Medicine. Burakoff will oversee efforts in cancer research and cancer genetics. The Medical Center said it plans to strengthen its clinical research facilities, to develop a dedicated unit for medical oncology in Tisch Hospital, and a new outpatient oncology unit. . . . **STEVEN FRIEDMAN** was appointed director of policy and quality initiatives at the National Coalition for Cancer Survivorship. Friedman worked six years with Aetna as manager of operational quality, three years for the National Committee for Quality Assurance as senior accreditation manager responsible for surveyor activities and new product development, and a year as a consultant to health-related companies. . . . **JONATHAN LEWIS**, a surgical oncologist and clinical investigator at Memorial Sloan-Kettering Cancer Center, was appointed vice president for medical affairs at Antigenics Inc., of New York City. Lewis will be responsible for the development, implementation, and strategy of the company's clinical trials programs. Lewis was the principal investigator testing Antigenics' lead product, Oncophage, in pancreatic cancer patients. He joined MSK in 1992 as a surgical oncology fellow.

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Business & Regulatory Report

Oncology Management:

Reimbursement Of Some Anticancer Drugs Expected To Drop Sharply Under HHS Policy

HHS has recalculated the "average wholesale price" of drugs utilizing 50 chemical compounds and is about to start reimbursement at adjusted, lower, rates.

The new policy will affect about 20 chemical compounds commonly prescribed to cancer patients, including cisplatin, cyclophosphamide, leucovorin, lupron, mitomycin, etoposide, 5-FU, vincristine and vinblastine.

Though a comprehensive comparison of the new prices and AWP is not available, observers say decreases in reimbursement will be particularly precipitous—50 percent or more—for multi-source drugs.

HCFA reduced the reimbursement scale following an investigation

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Product Approvals & Applications:

FDA Approves Large-Volume Processor For Cytyc's ThinPrep Pap Test Samples

Cytyc Corp. (Nasdaq:CYTC) of Boxborough, MA, said FDA approved its ThinPrep 3000 Processor, a fully automated system capable of unattended batch processing of ThinPrep Pap Test samples.

Cytyc said it has also submitted a pre-market approval supplement to its FDA approved ThinPrep 2000 System in October 1999.

The ThinPrep 3000 is designed for large volume laboratories and will complement the ThinPrep 2000 Processor, which can process the ThinPrep Pap Test as well as non-gynecological specimens, the company said.

* * *

Teva Pharmaceutical Industries Ltd. (Nasdaq: TEVA) of Jerusalem, Israel, said its Dutch subsidiary, **Pharmachemie B.V.**, received U.S. FDA final approval to manufacture and market Tamoxifen Citrate 10mg Tablets for metastatic breast cancer and the reduction of breast cancer incidence in high risk women. A patent infringement case relating to the product is pending in a US Federal District Court in Massachusetts, the company said. Teva expects a decision from the court on inequitable conduct.

Teva said that in granting final approval for Tamoxifen Citrate, the FDA has acknowledged that there is no entitlement to market exclusivity by any generic company. The issue of market exclusivity has been the

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Patient And Physician Groups Lobby Against Policy Change

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conducted by the Department of Justice. Altogether, the drugs on the new list represent about a third of Medicare spending for drugs.

If the administration plan proceeds as scheduled, the new scale will become effective Oct. 1. However, sources say, the drop may still be averted through legislation, most likely the House Republican version of the Medicare drug benefits bill, which was recently amended by Rep. Nancy Johnson (R-CT) to require HHS to study the reimbursement structure for oncology drugs before making changes.

The Administration's move is part of a four-year effort to cut reimbursement for drugs, particularly cancer drugs. First, in 1996, the Administration tried to take the markup out of oncology by reimbursing physicians on actual acquisition prices for drugs. However, this move was thwarted through the Balanced Budget Act of 1997, which fixed reimbursement at Average Wholesale Price minus 5 percent.

AWP, published in a compendium called The Red Book, generally represents the price paid by physicians before volume discounts and other incentives. Frustrated by Congress in its efforts to disregard AWP, the Administration decided to recalculate it.

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"This is the most immediate action we can undertake without undergoing the formal rule-making process," HHS Secretary Donna Shalala wrote in a May 31 letter to Rep. Thomas Bliley (R-VA), chairman of the House Committee on Commerce.

Efforts to peg reimbursement to actual acquisition cost may replace the Administration's proposal to reimburse at AWP minus 17 percent, Shalala wrote. That plan is included in the President's budget proposal for the fiscal year 2001.

Patient groups and oncology societies are lobbying against the adjustment to AWP.

"By seeking to redefine the meaning of AWP as used in the 1997 legislation, HHS would circumvent the intent of Congress in its establishment of reimbursement levels of 95 percent of AWP," the Cancer Leadership Council wrote in a letter to Rep. Bill Archer (R-TX), chairman of the House Ways and Means Committee.

"It does not seem to us that Congress intended to give HHS the flexibility to change reimbursement levels through administrative action by redefining AWP when Congress incorporated the traditional meaning of AWP into the very specific calculation of appropriate reimbursement," the council wrote in a letter dated June 8.

Taken to a logical extreme, if HHS adjusts AWP to equal the acquisition price, physicians may have to take a 5 percent loss on drugs they administer to Medicare patients.

The American Society of Clinical Oncology said the HHS policy "is not based on a sound understanding of the costs of providing quality cancer care, and will make it extremely difficult for physicians to provide office-based chemotherapy to people with cancer."

ASCO said that even under current rules, Medicare does not cover many of the costs of administering chemotherapy. The society said the government does not pay the costs of preparation and administration of chemotherapy, specialized equipment for mixing and storing the drugs, staff time involved in procuring the drugs, inventory costs, wastage and spillage, state taxes in several states, and unpaid coinsurance.

"Until Medicare rectifies the payment amount for chemotherapy administration, physicians will need to rely on drug payments to help cover the true costs of delivering the treatment," the ASCO letter said. "If their costs are not covered, the ability of physicians to provide services to cancer patients—and to carry on their practices—is at stake."

The ASCO statement is on the association's web site: http://www.asco.org. Shalala's letter describing the Administration's plans can is at the Committee on Commerce web site: http://com-notes.house.gov/cchear/hearings106.nsf/main. The list of drugs that will be affected by the proposal is on the web site of the Association of Community Cancer Centers: http://www.accc-cancer.org.

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University of Texas M. D. Anderson Cancer Center announced the opening of M.D. Anderson International-España, its first international affiliation and the first multidisciplinary full-service cancer center in Spain.

The affiliate consists of a hospital with inpatient and outpatient services and radiation therapy facility built to specifications and standards established by M. D. Anderson, the center said.

M. D. Anderson International-España is a venture of MDA Holding Spain, S.A., a Spanish investment consortium, and the M. D. Anderson Outreach Corp., a health care organization created in 1989 to open and expand access to the M. D. Anderson services, the center said.

MDA Holding Spain said it would develop and market an insurance product that will guarantee treatment at M. D. Anderson International-España and in Houston. The product will target approximately six million people in Spain who have private insurance through their employers.

The facility will be the only one in Spain where cancer patients can receive all of their diagnostic tests, inpatient and outpatient treatment and see all of their physicians at a single site, said to Martin Raber, senior vice president for strategic and business planning at M.D Anderson.

"Patients also will have access to many of the clinical trials offered at M. D. Anderson," said John Mendelsohn, president of M.D. Anderson." More than 100 patients come from Spain to M. D. Anderson Cancer Center in Houston every year, and many more would like to come but cannot because of the time and expense required."

The facility will house two new linear accelerators and a treatment planning system as well as an MRI, brachytherapy, CT scanner, mammography and ultrasound. All the radiology equipment is digital to allow for images to be transmitted throughout the Madrid center and to Houston, the center said.

In another development, M. D. Anderson said it is authorized to grant degrees to its students.

Following legislation passed by the 76th Texas Legislature and approval by the UT System Board of Regents and the Texas Higher Education Coordinating Board, M. D. Anderson is able to offer bachelor of science degrees in cytogenetic technology, cytotechnology, medical dosimetry, medical technology and radiation therapy. All five programs are accredited by their respective national credentialing agencies, the center said.

The current national vacancy rates in the five specialties range from seven percent to 14 percent, creating significant demand for persons trained in these areas, the center said.

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Varian Medical Systems Inc. (NYSE:VAR) of Palo Alto, CA, said it would acquire as a wholly-owned subsidiary, **Impac Medical Systems Inc.** of Mountainview, CA, a private information systems radiation and medical oncology management company.

Varian said the acquisition would offer customers health care information products for clinical, administrative, outcomes, and decision support purposes.

Under the agreement, the transaction will be through a pooling of interests. Varian said it would issue approximately 3 million common shares and 300,000 options in exchange for all IMPAC common and preferred shares and options, equating to an enterprise value of approximately $121 million and an equity value of approximately $135 million.

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Optx Corp. of Denver, CO., a change management and technology services company for the oncology marketplace and **Duke University Health System** said they have contracted to streamline and redesign oncology care services for Duke cancer patients.

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Genzyme Genetics (Nasdaq: GENZ) of Framigton, MA, said it has agreed to be a national participating provider of specialty genetic testing services to **Aetna U.S. Healthcare** members.

The contract covers the Aetna HMO-based plans, as well as other plans that purchase genetics testing and counseling benefits, the company said. Terms of the agreement were not disclosed.

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Icos Corp. (Nasdaq: ICOS) of Bothell, WA and **Texas Biotechnology Corp.** (Amex:TXB) of

Houston, said they have agreed to form a 50/50 owned joint venture, Icos-Texas Biotechnology, Limited Partnership, to develop and globally commercialize endothelin-A receptor antagonists for the treatment of a number of diseases including prostate cancer.

Both parties said they would equally fund the cost of research and development of second-generation endothelin antagonist compounds, commercialize resulting products, and share equally in the profits from this worldwide collaboration. Icos said will make milestone payments to Texas Biotechnology, as much as $55.5 million, for the development and commercialization of products.

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PETNet Pharmaceuticals Services Inc. of Knoxville, TN, said it agreed to exclusively provide **U.S. Oncology Inc.** with radiopharmaceuticals for its PET imaging sites. U.S Oncology operates one PET imaging site in Dallas and plans to open 30 new sites within the next two years, the company said.

"U.S. Oncology shares our vision of the potential of PET to foster early detection, accurate diagnosis and effective treatment of cancer," said Mark Rhoads, president and CEO of PETNet.

PET/molecular imaging, a metabolic imaging procedure, which employs intravenously administered radiopharmaceuticals.

In a related development, U.S. Oncology and CTI Inc., a majority shareholder of PETNet, said they have signed a separate agreement whereby CTI will provide U.S. Oncology practices with ECAT EXACT PET scanner, a system that excels at brain and whole-body imaging, the companies said.

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Eli Lilly (NYSE: LLY) of Indianapolis, IN, said it is expanding its oncology sales force in the U.S by more than 250 percent.

"This is the largest single investment ever made in our oncology sales force and represents our commitment to becoming one of the top three oncology companies in the next five years," said Gino Santini, president of U.S. operations and global marketing for Lilly.

Santini said the sales of Gemzar (gemcitabine HCl) are among the reasons for the espansion. Gemzar is approved in the U.S. for the treatment of pancreatic cancer and in combination with cisplatin for the treatment of non-small cell lung cancer, the company said.

Last year, global sales of Gemzar were $456 million.

Clinical Trials:

Sustained-Release Leuprolide Under Study In Phase III Trial

Atrix Laboratories (Nasdaq: ATRX) of Fort Collins, CO, said it has begun a multi-center phase III trial of Atrix Atrigel drug delivery system to administer a 30-day sustained release of leuprolide acetate subcutaneously. The therapy is being tested in advanced prostate cancer patients.

"Testosterone levels below 20 nanograms per deciliter (ng/dL)—level well below castration—are ideal," said Steve Garrett, vice president of clinical research at Atrix. "Analysis of the 36 patients who have now completed our study, show levels below 20 ng/dL."

In addition to the 30-day product in clinical development, Atrix said it received FDA approval for its investigational new drug applications to study Atrigel products releasing leuprolide for 90 and 120 days, respectively.

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Cantab Pharmaceuticals plc (Nasdaq: CNTBY) (LSE: CTB) of Cambridge, England, an immunotherapy and gene delivery development company, said it has begun a phase I trial of Ta-cin, a vaccine for cervical dysplasia.

The study, which is being conducted in The Netherlands on 40 healthy individuals, is designed to assess vaccine safety, tolerability, and to measure immunological responses. Volunteers receive a course of three monthly injections using a high, medium or low dose formulation.

The vaccine is based on a genetically engineered fusion protein derived from HPV, and is designed to stimulate the immune system to destroy cervical cells that are infected with HPV16, the type most commonly found in advanced stages of cervical dysplasia, the company said.

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ImClone Systems Inc. (Nasdaq: IMCL) of New York, said it has begun a phase I trial of its anti-angiogenesis agent, IMC-1C11, for metastatic colorectal carcinoma.

IMC-1C11 is a chimerized monoclonal antibody that inhibits the KDR receptor (VEGFr) on vascular endothelial cells by blocking binding of the Vascular Endothelial Growth Factor (VEGF) to the receptor, the company said. KDR is a key receptor associated with tumor angiogenesis.

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Norton Healthcare Cancer Center of Louisville, KY, said it has initiated a phase III trial in its Louisville Oncology Research Program of adenoviral p53 gene therapy for recurrent/refractory squamous cell carcinoma of the head and neck.

The study would determine whether the gene therapy would control tumor growth rate and improve patient survival when compared to chemotherapy, the company said.

The trial, sponsored by **Aventis Pharmaceuticals** and **Introgen Therapeutics** through their collaboration to develop and commercialize gene therapy products, will enroll 240 patients at more than 60 sites across the U.S., Canada and Europe. Half the patients will receive intra-tumoral injections of the gene therapy, and the other half will receive intravenous methotrexate, the company said.

In phase II trials of 170 patients with recurrent/refractory scchn, tumor growth control was demonstrated in 26 percent of patients, the company said. In a subgroup analysis, evidence of anti-tumor activity was shown in approximately 60 percent of individually evaluated tumor lesions. Activity was seen in patients with both p53 mutated and non-mutated tumors.

A p53 therapeutic may be used alone or in combination with surgery, chemotherapy and radiation therapy and appears to program the tumor cells to die or stop growing. The expression of the normal p53 gene makes the cancer cell more sensitive to the effects of DNA damage by radiation and chemotherapy and thus more easily killed by these agents, the company said.

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Onyx Pharmaceuticals Inc. (Nasdaq: ONXX) of Richmond, CA, and **Warner-Lambert Co.** (NYSE: WLA) said they have begun a phase III trial of CI-1042 (ONYX-015) for the treatment of recurrent head and neck cancer.

CI-1042 is a tumor-selective, oncolytic, biologic therapy engineered to replicate in the presence of tumor tissue, the companies said

The randomized two-arm trial of 300 patients will compare intratumoral injection of CI-1042 plus standard chemotherapy (5-flurouracil and Cisplatin) versus chemotherapy alone, the companies said. The endpoints will include tumor responses, progression-free survival, durable tumor responses, patient quality of life measurements and overall survival, the companies said.

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SafeScience Inc. (Nasdaq: SAFS) of Boston said it had begun a phase II trial of the carbohydrate compound, GBC-590, for colorectal carcinoma.

The trial will determine safety and efficacy in patients who have failed no more than two prior regimens of chemotherapy, the company said.

"GBC-590 has been implicated in several different modes of anti-tumoral activity," said Thomas Cartwright, principal investigator of the Ocala Oncology Center. "Preclinical studies have indicated that GBC-590 may shrink primary tumors. Additionally, GBC-590 binds to the galectin-3 receptor on tumor cells. The site has been shown to be involved in the metastasis of tumors."

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Techniclone Corp. (NASDAQ:TCLN) of Tustin, CA, said its phase II study of Cotara for the treatment of brain cancer would expand to include the University of Miami and will continue to add sites to increase enrollment.

Medical University of South Carolina, University of Utah, Temple University and Carolina Neurosurgery and Spine Associates are active sites in the trial, the company said. Aldo Serafini professor of radiology and medicine at the University of Miami School of Medicine is the lead investigator.

Deals & Collaborations:

Celgene Signs CRADA With NCI For Development Of CDC-501

Celgene Corp. (Nasdaq: CELG) of Warren, NJ, said it has signed a letter of intent for a cooperative research and development agreement with NCI for the clinical and preclinical development of its compound CDC-501 and other ImiDs.

IMiDs are a group of novel, patented, structural analogues designed and synthesized based on the biological activity and structure of thalidomide. The orally available drugs appear to have greater immunological activity in preclinical models, specifically their ability to inhibit the undesirable overproduction of TNF-alpha, yet may have fewer side effects than the parent compound, the company said.

The five-year research program would determine the compounds maximum tolerated dose, cytotoxicity, pharmacokinetics, and characterize the side effect profile and evaluate the effect of IMiDs on several biological endpoints, the company said.

Two phase I trials and a phase II trial would be performed, the company said. The NCI team will be led by William Figg, Howard Fine and Robert Yarchoan, the company said.

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Celsion Corp. (AMEX:CLN) of Columbia, MD, said **Massachusetts Institute of Technology** has agreed to exclusively license its breast cancer treatment technology to Celsion.

The technique, developed by Alan Fenn, senior staff member of the Advanced Electromagnetic Systems Group at Lincoln Laboratory, MIT, uses microwave signals to heat and kill cancer cells in breast tissue.

A phase I study with the first group of seven patients is complete; another group of three patients will begin treatment soon. A phase II trial, which could be completed within the year, will treat early-stage or advanced breast cancer.

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Endocare Inc. (Nasdaq: ENDO) of Irvine, CA, said **Johns Hopkins** has begun both clinical and research programs to study targeted cryoablation in treating prostate cancer and renal disease.

Ronald Rodriguez, assistant professor of urology at Johns Hopkins, will head a research project on the immunologic effects of cryoablation to augment gene therapy approaches to advanced prostate cancer, the company said.

A team of Johns Hopkins urologists has been evaluating cryosurgery for small peripheral renal masses and is now adopting the Endocare Cryocare system to advance the research, the company said. The team is evaluating combining cryosurgery with certain forms of gene therapy in treating advanced-stage prostate cancer for clinical trials.

In a related development, Endocare said it would open international training centers at FMMU Hospital in Guangzhou, China, Hospital das Clinicas at the University of Sao Paolo, Brazil and Royal Surrey County Hospital in Guildford, UK, each of which is affiliated with a leading university teaching hospital.

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Eos Biotechnology Inc. of South San Francisco, said it has entered into an alliance with **Aventis Pasteur** of Lyons, France, a wholly-owned subsidiary of **Aventis SA**, to develop genomic based cancer vaccines.

Eos said it would supply its genomics approach to identify, select and validate targets for vaccine products and Aventis Pasteur would contribute its vaccine development expertise.

Under the multi-year agreement, Aventis Pasteur would obtain an exclusive license to develop vaccines against selected targets identified by Eos in return for an up-front payment and research and development funding. In addition, Eos will receive milestone and royalty payments on products commercialized by AP, the company said.

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Ligand Pharmaceuticals Inc. (Nasdaq: LGND) of San Diego, said it would issue to **Elan Corp. plc** (NYSE:ELN) of Dublin, Ireland, 367,183 shares of its common stock for the Elan submission of a new drug application FDA for Morphelan Rapid Onset Extended Release capsules, a once-daily, modified-release, oral dosage form of morphine for the management of pain in oncology and HIV-positive patients.

With the issuance of these shares, Elan and its affiliates will own approximately 12.5% of Ligand's outstanding common stock (17.6% on a fully diluted basis), the company said.

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Maxim Pharmaceuticals (Nasdaq: MAXM) (SSE: MAXM) of San Diego, said its acquisition of Cytovia Inc., a privately held biopharmaceutical research company focused on the discovery and development of apoptosis inhibitors and activators, is complete.

The Cytovia technology base includes proprietary drug candidates in oncology, oral mucositis and cardiovascular disease, and a proprietary high-throughput screening process for other apoptosis-targeted drug candidates, the company said.

Under the terms of the acquisition, Maxim said it would issue approximately 1.5 million shares of its common stock, or seven percent of its total post-transaction shares outstanding, to the former shareholders of Cytovia.

Maxim said it is obligated to file a registration statement within 30 days to allow resale of the common stock.

However, the Cytovia shareholders have entered into a lock-up agreement that prevents them from currently selling any of theMaxim common stock received in this acquisition. After three months, 25 percent of these shares are released from the lock up agreement, and an additional 25 percent are released at the end of each subsequent three-month period, the company said.

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Myriad Genetics Inc. (Nasdaq: MYGN) of Salt Lake City said it has discovered a prostate cancer susceptibility gene prompting a $1 million payment from **Schering-Plough Corp.** under the 1997 research collaboration agreement.

According to the agreement, Myriad said it retains all diagnostic product rights to the gene and will receive a royalty on all sales of relevant therapeutic products developed by Schering-Plough. U.S. and foreign patents have been filed.

To identify the gene, Myriad said its researchers employed a proprietary form of linkage analysis that tracks a disease susceptibility gene to its location on a specific chromosome. Based on its analysis of prostate cancer families, Myriad said it determined that inherited mutations in the gene might significantly increase the risk of prostate cancer. The mutation profile of the new gene indicates the potential to form the basis of a prostate cancer susceptibility test, the company said.

The discovery of the prostate cancer gene culminates a research project between Myriad and its prostate cancer family database and linkage collaborators, which include research groups led by Lisa Cannon-Albright, University of Utah, Johanna Rommens, University of Toronto and Jacques Simard and Fernand Labrie, University Hospital and Endorecherche, the company said.

In another development, Myriad Genetics Inc. said it had collaborated with the **Pharmacia Corp. G.D. Searle & Co.** unit, to identify two proteins, which Searle is evaluating

The proteins were identified with the Myriad high-throughput, automated ProNet technology, the company said

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NaPro BioTherapeutics Inc. (Nasdaq: NPRO) of Boulder, CO, said it has expanded its development and marketing relationship for paclitaxel with **F. H. Faulding & Co. LTD**., the largest pharmaceutical company in Australia.

The agreement would include Central America, South America and Mexico, South Africa and additional territories in Southeast Asia and the Middle East, the company said. Faulding has received marketing approval and has begun selling paclitaxel in Mexico and Brazil.

Faulding has exclusive development and distribution rights to NaPro paclitaxel in some 75 countries worldwide and has applications for marketing approval in place for an additional dozen countries with more to follow, the company said.

NaPro said its sales to Faulding for commercial use in their territory increased from $2 million in 1995 to $5.1 million in 1999.

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OSI Pharmaceuticals Inc. (Nasdaq: OSIP) of Uniondale, NY, said they will receive all development and marketing rights for EGFR inhibitor CP-358, 774 (OSI-774) from **Pfizer Inc.** (NYSE: PFE) to fulfill FTC requirements for the Pfizer merger with **Warner-Lambert Co.** (NYSE: WLA).

Warner-Lambert is developing an EGFR inhibitor CP-358,774 (OSI-774,)a potent, selective and orally active inhibitor of the EGFR oncogene. EGFR inhibitors are considered among the most promising new cancer treatments under development, the company said.

Under the agreement with Pfizer, OSI Pharmaceuticals said it will receive a royalty-free license to all rights for the further development and commercialization of CP-358,774 (OSI-774). Pfizer continues to coordinate the phase II trials in ovarian, head and neck and non-small cell lung cancer through a transition period of up to 6 months.

Pfizer will also provide OSI with its inventories of finished product, bulk drug and production intermediates, the company said.

OSI said enrollment is complete for a 30 patient single agent open label salvage study in ovarian cancer and approximately 45 patients in non-small cell lung cancer and is ongoing for a similar study involving 100 patients in head and neck cancer. Patients in these studies have advanced cancer and have failed standard treatment regimens, the company said.

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Panacea Pharmaceuticals Inc of Rockville, MD, said it has signed both a license agreement and a collaborative research agreement with **Rhode Island Hospital/Brown University** for human aspartyl (Asparaginyl) beta-hydroxylase.

The over-expression of HAAH is associated with the transformation of normal cells to malignant tumors, the company said. In animal studies, levels of the enzyme are markedly increased in tumors, the company said.

When the gene for this enzyme is inserted into normal cells and the over-expression of the enzyme is initiated, the cells become cancerous. The injection of cells containing the gene for the enzyme into mice

causes tumor formation whereas non-transfected cells do not produce tumors, the company said.

Studies show the over-expression of HAAH in 100% of human cholangiocarcinomas, but not in regenerating bile duct cells. Moreover, increased levels of HAAH have been observed in breast cancer, colon cancer, and hepatocellular carcinomas, some of the most prevalent tumors in the world.

Panacea said its is developing HAAH-based diagnostic tests for glioblastoma multiforme, hepatocellular carcinoma, cholangiocarcinoma, and pancreatic cancer.

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PPD Discovery, of Menlo Park, CA, a wholly-owned subsidiary of **PPD Inc.** (Nasdaq: PPDI) of La Jolla, CA, and **Agouron Pharmaceuticals Inc**., a wholly owned subsidiary of **Warner-Lambert Co.** (NYSE: WLA) said they have formed an alliance to identify new targets for selectively eradicating cancer cells.

The collaboration will focus on discovery and validation of novel drug targets, the companies said.

PPD Discovery said its proprietary functional genomics platform, the GSX System, will be used to perform high-throughput genome wide screening for genetic suppressor elements capable of inducing apoptosis of a tumor cell.

GSEs mimic drug effects by modulating the expression or biochemical activity of a specific target protein, the company said.

Under the agreement, Agouron will provide an up-front payment and support research at the PPD Discovery genomics facility. PPD Discovery will receive research and development milestone payments and royalties on sales of Agouron products from the collaboration. PPD Discovery will retain certain rights to pharmacogenomic and diagnostic applications and products with Agouron receiving royalties on sales of any diagnostic and pharmacogenomic products resulting from the collaboration, the companies said.

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Siemens Medical Systems of Iselin, NJ, and **NMR-Center of Massachusetts General Hospital** in Cambridge, said have signed a five-year strategic collaboration in advanced neuro MR research.

The radiology, neurology and psychiatry teams will use the Siemens advances in 3 Tesla engineering, gradient amplifier and coil technology, as well as multi-channel high bandwidth RF capability, said Bruce Rosen, director of the NMR-Center at MGH.

"The Siemens MR hardware and software platform is truly impressive and will help us to quickly bring our ideas to reality," said Gregory Sorensen, head of the neurology team at the NMR-Center. "We will first focus on brain perfusion post-processing, diffusion tensor imaging, and a BOLD MRI toolkit."

The Siemens equipment used in the first phase of the agreement includes investigational devices of a 3 Tesla whole body scanner, two 3 Tesla MAGNETOM Allegra dedicated brain systems, as well as high performance 1.5 Tesla Magnetom Sonata systems, the company said.

The 3T Whole Body product will be the result of the recently announced strategic alliance in very high field imaging between Siemens and Bruker Medical.

The current agreement is valued at well over $10 million, the company said.

Approvals & Applications:

FDA Approves Marketing Of Respiratory Gating System

(Continued from page 1)

subject of considerable litigation among several generic drug companies and the FDA, the company said.

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Varian Medical Systems Inc. (NYSE:VAR) of Palo Alto, CA, said FDA has approved the marketing and distribution of the CT option for its RPM Respiratory Gating System, determining it a class one device exempt from pre-market notification requirements of the Food Drug and Cosmetic Act.

The system increases the accuracy and efficacy of cancer radiotherapy by adjusting for tumor movements caused by breathing and has "gates" that turn the radiation beam on or turn off when a tumor in the chest and abdomen moves outside a prescribed target area, the company said.

The CT option extends respiratory gating to the CT scanner so that movements recorded during the diagnostic imaging process can be correlated via treatment planning with the respiratory gating system that controls the Varian Medical System Clinic medical linear accelerators, the company said.

Varian said its gating solution is low-cost, non-invasive, and uses highly reliable optics to triangulate respiratory motion with sub-millimeter accuracy.

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