THE CANCER LETTER INTERACTIVE

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"Dear ASCO Member" Letter From Klausner Attempts To Rescue Flagging BMT Trial

In a letter to members of the American Society of Clinical Oncology, NCI Director Richard Klausner urged physicians to continue to enroll patients in an NCI-sponsored randomized trial testing bone marrow transplantation in women with four or more positive lymph nodes.

"The rationale behind the treatment approach remains sound," Klausner said in a letter dated May 19. "While there are experts who feel existing data suggest that ongoing trials will be negative, others are more optimistic. The only way to resolve this disagreement is through

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In Brief:

McKay Retires As Fox Chase Executive, Is Succeeded By Donald Leedy As VP

FRANCIS McKAY, executive vice president of Fox Chase Cancer Center and a leader in the center's founding, announced his retirement after 37 years at the center. McKay will maintain a partial appointment as vice president for extramural activities including the Fox Chase Network of community hospital-based cancer centers, the National Comprehensive Cancer Network of national cancer centers, and development of the Fox Chase-Temple University Cancer Program. Fox Chase Cancer Center President **Robert Young** appointed **Donald Leedy,** vice president for finance and treasurer of the center since 1981, to succeed McKay as vice president-administration and chief operating officer, effective June 1. . . . **GUY MCKHANN,** former chairman of the Johns Hopkins University Department of Neurology and founding director of the Hopkins Mind/Brain Institute, was named associate director for clinical research at the National Institute of Neurological Disorders and Stroke. McKhann will serve as acting clinical director for intramural research. "He will strengthen our efforts to recruit a new generation of physician scientists and enhance collaboration among the many components of neuroscience," said NINDS Director **Gerald Fishbach**. . . . **CRAIG MELLO**, assistant professor of cell biology at the University of Massachusetts Medical School, was named Howard Hughes Medical Institute Investigator. Mello, known for his contributions to human development and cancer with his genetic work on the worm C. elegans, is an investigator at the UMass Cancer Center. . . . **JOHN POTTER**, head of the Cancer Prevention Research Program at the Fred Hutchinson

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As Interest Wanes, NCI Says BMT Remains A Viable Option

(Continued from page 1)

participation in large, carefully monitored clinical trials."

The ups and downs of S9623, an intergroup trial led by Southwest Oncology Group, reflects the 10-year battle between hype and science over the role of high-dose chemotherapy and bone marrow transplantation as a therapy for breast cancer in the U.S.

More importantly, the trial's current woes are illustrative of the uncertain state of transplantation today.

S9623 is a second-generation BMT trial. Its structure reflects the lessons learned from earlier trials, which asked pure research questions, but, alas, failed to accrue patients rapidly. Unwilling to be randomized to less aggressive treatment, many women obtained their transplants off protocol, or in single-institution phase II trials.

As trials failed to accrue, and as the transplant business boomed, clinical researchers realized they could not always afford pure research questions. Therefore, instead of comparing higher and lower doses of the same drugs, S9623 compares two aggressive regimens: intensive sequential doxorubicin, paclitaxel, and cyclophosphamide with G-CSF support vs. doxorubicin and cyclophosphamide followed by STAMP I or STAMP V, standard transplant regimens requiring autologous stem cell rescue. STAMP I consists of cyclophosphamide, cisplatin, and carmustine, and STAMP V consists of cyclophosphamide, cisplatin, and thiotepa.

Since both arms of the trial were viewed as cutting-edge in 1996, women were willing to accept randomization, and by the spring of 1999, the trial accrued over 500 women with at least four positive lymph nodes, about half of the enrollment target.

The trial's lucky streak ended last spring, after two other cooperative groups reported data that indicated that transplantation was not superior to standard chemotherapy. One of the studies, Cancer and Leukemia Group B trial 9082, was also conducted in a high-risk adjuvant setting, in women with 10 or more positive nodes. The other trial, the Philadelphia Intergroup Study (PBT-1), was conducted in metastatic disease.

The negative studies were presented at last year's plenary session at ASCO (**The Cancer Letter**, May 28, 1999). Following these presentations, enrollment in S9623 dropped dramatically. In recent months, the trial has been accruing two or three women a month, said Jeff Abrams, a clinical researcher who coordinates breast cancer trials at the NCI Cancer Therapy Evaluation Program.

"Ever since the ASCO 1999 meeting when preliminary results from several transplant trials did not show a survival advantage, enrollment has suffered," Klausner wrote in his letter to the ASCO annual meeting, held in New Orleans earlier this month.

"Importantly, this trial tests the question in a different subset of patients than did prior NCI-sponsored trials, and accordingly the preliminary results of these earlier trials may not be applicable to this subset," wrote Klausner, who did not attend the society's conference in New Orleans earlier this month.

The NCI push for continuing enrollment in trials of the controversial procedure was supported by two patient groups, the Susan G. Komen Breast Cancer Foundation and the National Alliance of Breast Cancer Organizations.

In addition to the Klausner letter, NCI issued a press release titled, "Don't Write off High Dose Chemotherapy for Breast Cancer, Experts Say."

Fran Visco, a member of the President's Cancer Panel and president of the National Breast Cancer Coalition said the research questions asked in the

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trials, if relevant in 1996, are less relevant today.

"The field of breast cancer has moved on," Visco said to **The Cancer Letter**. "We are looking at the molecular basis of disease, targeted interventions, anti-angiogenesis compounds, and the like, and as patient advocates, we are interested in looking at more innovative questions."

NBCC has regarded transplantation as an unproven therapy, taking the position that women who choose it should do so only in the context of clinical trials. However, for NBCC, support for BMT trials does not translate into demands for definitive answers on transplantation.

"We understand the scientists' need to get the answers, but as patient activists, we don't think that every question in science necessarily warrants allocation of precious resources, the most important of which is women's lives, to answer," Visco said.

"Not a Third Rail"

Transplanters were pleased by Klausner's statement of support for the SWOG trial. "I took the statement from Klausner as a step in the right direction," said William West, chairman of Response Oncology Inc., a company that operates transplant centers. "It's not a third rail of oncology; it's an important area of research."

West said that following the release of data on BMT last year, breast cancer referrals to the transplantation centers operated by the company dropped by two-thirds. "The media frenzy has made it politically incorrect to even suggest high-dose," West said to **The Cancer Letter**. "That needs to change. High dose is still an important study option."

Looking at the BMT debate from the methodological perspective, I. Craig Henderson, senior medical advisor at Alza Corp. and adjunct professor of medicine at the Unversity of California at San Francisco, said he is delighted to see all players acknowledge the uncertain value of the procedure.

"If you have too much certainty—even if it's based on belief rather than on fact—on either side, you can't do a clinical trial," Henderson said to **The Cancer Letter**. "Until last year, we were getting too much certainty that BMT worked, without enough data. Then, last year, we swung back to the other side."

The much-needed veil of uncertainty was enhanced through presentation of preliminary results from an 885-patient phase III adjuvant study from the Netherlands, Henderson and other observers said.

After analyzing the data from about a third of the randomized patients, the study found a 15-percent advantage in event-free survival and a 10-percent advantage in overall survival on the transplant arm. Treatment mortality was about 1 percent.

"What the Dutch data did, together with the Klausner letter, is reintroduce balance between the two extremes," Henderson said. "I think we swung too radically in one direction, then maybe too far back other direction. Maybe we are coming back so we are at equipoise now."

The Netherlands trial, by S. Rodenhuis *et. al.*, is described in the ASCO 2000 annual meeting program book, abstract 286, and is available on the society's web site, http://www.asco.org.

Old Questions? New Questions?

Believers, skeptics, and those trying to keep an open mind about BMT agree on one point: the days when patients accepted transplantation as the optimal care, while insurers grudgingly shelled out the funds, are gone forever.

"I think there will be a lot less enthusiasm [for BMT] off-protocol," said Response Oncology chairman West. "A lot of that was driven by the patients themselves, and I think the patients have become more savvy, and realized that we need to answer questions in randomized trials."

Klausner's plea on behalf of the SWOG trial is unlikely to legitimize the procedure off-protocol, observers on both sides of the spectrum agree.

"I think the transplanters have seen the light and realized that unless they complete phase III trials, there will not be any scientific basis for the therapy," said Abrams. "They are eager to participate in randomized trials now, because they are not getting referrals otherwise. Had this current enthusiasm for randomized trials among transplanters existed in the 1990s, we wouldn't be in this position today."

Following the lead of Aetna/US Healthcare, insurers have been driving patients to institutions involved in bona fide randomized trials, observers say (**The Cancer Letter**, Business & Regulatory Report, February). Though this shift has not been studied formally, anecdotal accounts are persistent. "We hear this from transplanters at every meeting we go to," Abrams said.

Response Oncology chairman West agrees that transplanters need to get involved in trials. "If there is any good to come of this, it probably is that the marketplace will be more attuned to the role of

randomized trials," West said to **The Cancer Letter**. "We need the next generation of questions. For instance, one big question is the role of Taxol. I notice with interest that some opponents of high-dose believe that perhaps Taxol will deliver some of the benefits of the high-dose platform. I think a very interesting corollary question is, will the addition of Taxol enhance the benefit with the high-dose platform?"

Though of keen interest to transplanters, these questions do not necessarily excite the peer reviewers at NCI-funded cooperative groups. The groups are interested in finishing the ongoing high priority trials, not starting new ones.

"The community of non-transplanting medical oncologists, which is a subset of the whole (albeit the largest one), basically are taking an I-am-from-Missouri-you-will-have-to-prove-it-to-me stance before wanting to go ahead with new trials of transplantation," said George Sledge, a breast cancer expert at Indiana University Hospital and a member of the FDA Oncologic Drugs Advisory Committee.

According to last year's data, transplantation is not seen as promising for stage IV disease, a setting where most transplants in the U.S. have been performed.

In earlier-stage disease, skeptics are awaiting the results of EST-2190, a phase III trial of adjuvant CAF (cyclophosphamide, doxorubicin, and fluorouracil) vs. adjuvant CAF followed by intensification with high-dose cyclophosphamide and thiotepa plus autologous stem cell rescue in women with stage II/III disease who have 10 or more positive nodes.

The trial closed last August, and the results are likely to emerge within a year-and-a-half.

Why Aren't They Enrolling?

Why aren't women enrolling in the BMT trials?

Is it because of press coverage of the recent underwhelming results of transplantation? Or is it because physicians have stopped recommending transplantation as a reasonable treatment option?

Recently, NCI and the National Alliance of Breast Cancer Organizations polled 925 women between ages 34 and 75 to assess the public perception of transplantation.

About half the women surveyed said they were aware of bone marrow transplantation, and about half of those women said they would be very likely to consider that treatment if they developed breast cancer.

"The survey results show that women have not written off transplant as an option," Amy Langer, NABCO executive director, said in an NCI press release. The same press release quotes Susan Braun, president and CEO of the Susan G. Komen Breast Cancer Foundation, a group that supports the trials as well as continued reimbursement of the procedure off-protocol (**The Cancer Letter,** April 16, 1999). "It would be shortsighted to close the door on all transplant trials for breast cancer based on the information we have right now," Braun said.

Abrams said the survey indicates that S9623 is not accruing patients because physicians are not recommending transplantation as an option.

"At least from that small survey, it seems that patients are not totally against consideration of transplantation," Abrams said to **The Cancer Letter**. "It really seems that they are not being offered trials of transplantation by the medical community. It is the physician who has to bring this up if it's going to be a possibility."

NBCC president Visco disagrees.

"Patient advocacy has moved beyond just arguing in support of what your doctor tells you to do," she said. "Patients today are much more likely to educate themselves and get their own information about options. In a trial like this, we are dealing with a non-metastatic population, looking at a highly toxic option in a world where there are new approaches to the disease."

Ethical, Well-Designed, But Is It Useful?

Nearly all oncologists acknowledge that it would be useful to complete the high priority trials, including S9623. Similarly, these physicians agree that the trial is ethical and well designed. However, in the four years since the trial was launched, science has progressed, altering the scientific questions, skeptics say.

"If you ask me, do I consider transplant the wave of the future, in the sense that many people did 10 years ago, the answer is no," said Sledge. "I think we are moving into an era where highly targeted biologic therapy is probably going to replace bludgeon therapy."

Matthew Ellis, a breast cancer expert at Georgetown University, said he put two patients on the trial more than two years ago. "It made sense when it was designed," Ellis said of the trial. However, the idea of using stem cell technology simply to support higher doses of non-specific therapy

is not as intriguing as it was a decade ago, or even two years ago, said Ellis, who is moving to Duke University to head the breast cancer program.

"The hope for the future of this technology is that we can use stem cells to support some other kind of novel breast cancer therapy, perhaps immunotherapy or vaccine therapy," Ellis said. "The whole philosophy of breast cancer treatment is moving toward more targeted therapy, either gene-targeted therapy, or targeting the immune system, and not just using more non-specific therapies, because we know that it hasn't brought us much bang for our buck. It's brought us some, but we are up against the limit of what chemotherapy can do."

Ellis said the dispute is a case study in how not to advance science. "The whole story is a big lesson in how vested interest and biased opinion interferes with the scientific process in both pro- and anti-transplant camps," Ellis said to **The Cancer Letter**. "We must practice evidence-based medicine, and if we offer a treatment with uncertain or marginal benefits, we must be completely honest in order to help the patient weigh the risks and benefits of unproven or experimental therapy."

Southern California oncologist and ODAC member Douglas Blayney said he is not spending much time worrying about the questions asked in S9623.

"The question is scientifically valid, but old," said Blayney. "It was the question that was appropriate at the time, and it should have been answered a long time ago."

Blayney said STAMP I and STAMP V may be too toxic to use in this population. "I think we can be a little more sophisticated about what to use," he said. "I think there are a lot of less toxic, different drugs that might be used, and a lot of better ways to generate stem cells than there were when the trial was designed."

Blayney said that he discusses transplantation as an option for his breast cancer patients. "I tell them that trials evaluating transplants are underway, and, certainly, I could refer them across town, if they are interested," said Blayney, whose practice, Wilshire Oncology Group, is part of the University of California at Los Angeles clinical trials network.

In the past 18 months, none of Blayney's patients have chosen transplantation. "Many breast cancer patients have a keen understanding of the issues in the field, and often are reluctant to undergo transplantation," Blayney said.

NCI's Abrams said the question asked in S9623 remains compelling.

"If I had a patient with four or more nodes who wanted an aggressive approach to therapy, that trial would certainly be among the top things I would talk to her about," Abrams said. "Although targeted therapies represent a great hope for the future, they offer little hope to patients with four or more lymph nodes today. NCI trials currently using these newer approaches are limited, and targeted approaches are often tumor-specific, so a majority of patients battling breast cancer now don't qualify for these trials.

"Transplant remains a viable option for a majority," Abrams said.

Transplanters: A Secession In The Making?

As demand for transplantation drops, reliance on NCI-sponsored randomized clinical trials may not be enough of a lifeline for transplanters.

Believers in the strategy find themselves unable to proceed to answering new questions until answers emerge to questions posed years ago.

After those questions are answered, transplanters will still have to face tough competition from researchers developing other approaches to the treatment of breast cancer.

Over the past year, transplanters have been working to form an independent consortium of academic and community centers and private groups focused on asking the new generation of questions involving high-dose chemotherapy for breast cancer.

Sources said efforts to form this consortium are led by William Peters, director of the Barbara Ann Karmanos Cancer Institute, and one of the pioneers of transplantation.

"Bill Peters is putting together a new consortium, and we are anxious to participate," West said. Originally, studies considered by this consortium were going to include an evaluation of the regimen developed by South African researcher Werner Bezwoda.

However, recent revelations that Bezwoda's data were fraudulent presented a setback to the fledgling consortium (**The Cancer Letter**, Feb. 11). "The Bezwoda debacle was a blow to this new consortium," West said. "The protocols are being rewritten, and we are simply waiting for their advice as to how we might interface and participate."

Peters' institution was in the midst of a regular site visit by NCI this week, and he could not be reached for comment.

Professional Societies:

ASCO Selects Three Cities For Quality of Care Study

NEW ORLEANS—The American Society of Clinical Oncology said that hospitals in Los Angeles, Houston, and Cleveland would be the first to participate in its study to explore the feasibility of developing a national monitoring system for the quality of cancer care in the U.S.

It is expected that additional cities will be chosen to participate in the pilot study in the coming months.

The 18-month pilot study will assess the feasibility of a national cancer care monitoring system and develop a prototype for such a system, by initially examining the care received by a sample group of 300 breast and 300 colorectal cancer patients.

A panel of ASCO physicians, patient advocates and other health experts will oversee the study, which will be conducted by researchers at Harvard University and the RAND Corporation.

"Beginning our research in Los Angeles, Houston, and Cleveland will provide a solid foundation of cancer care in the U.S.," said Joseph Bailes, president of ASCO. "What we learn in the first stage of this study will provide the groundwork and the strategy to develop a national system to help the cancer community ensure that patients nationwide receive the highest quality of care."

Using the National Cancer Data Base, Harvard and RAND researchers will review patient medical records to better assess the level of care given to each patient, including the type of treatment provided and the kind of follow-up received. In addition, researchers will conduct patient surveys to help understand patients' treatment experiences, the type of care received, where that care was received, insurance status and other information. All patient information will be kept strictly confidential.

"This study is a constructive response to the Institute of Medicine April 1999 report on 'Ensuring Quality Cancer Care,' which called for improved information about the quality of cancer care nationwide," said Joseph Simone, co-author of the IOM report. "I applaud ASCO's initiative in taking a leadership role so quickly, and at such a critical time."

The Susan G. Komen Breast Cancer Foundation is the major sponsor of the program, providing $1 million in funding towards the study. "We'd like to thank the American Society of Clinical Oncology for its vision and leadership in addressing this important issue," said Nancy Brinker, Founding Chair of the Komen Foundation. "Our commitment to patients and their families is what led the Komen Foundation to partner with ASCO and to help fund this quality of care initiative. What we learn from this initiative has the potential t impact each and every woman diagnosed with breast cancer in the future."

"ASCO has launched this Quality Study to better serve the thousands of cancer patients faced with this life-threatening illness," said Ellen Stovall, executive director of the National Coalition for Cancer Survivorship. "It is vital that a patient's treatment plan and experience receive this high caliber of attention and review by the largest organization of physicians who treat cancer patients."

ASCO is joined in the study by the American College of Surgeons, the Society of Surgical Oncology, the American Society for Therapeutic Radiology and Oncology, the Society of Gynecologic Oncologists, and the Oncology Nursing Society. Bristol-Myers Squibb, Amgen Inc., Aventis Pharmaceuticals, Agouron Pharmaceuticals Inc., Ortho Biotech, Immunex Corp. and the National Pharmaceutical Counsel also contributed to the funding of the study.

NCI Programs:

Early Detection Network Completes Initial Funding

NCI has awarded $18 million in first-year funding for the Early Detection Research Network, which brings together dozens of institutions to search for and evaluate new ways of testing for early cancer and for cancer risk.

Thirteen new grants are being awarded to three of the four network components: Clinical and Epidemiological Centers, Biomarker Validation Laboratories, and a Data Management and Coordinating Center.

Eighteen Biomarker Developmental Laboratories received $8 million in grants last fall. The network's Steering Committee will use $2 million in core funding to manage collaborative activities.

"Advances in cancer genetics, protein analysis, and other fields offer potential new biomarkers that one day may reduce the burden of cancer," said Sudhir Srivastava, chief of the Cancer Biomarkers Research Group in the NCI Division of Cancer Prevention. "Before they can move from the lab to

the clinic, these biomarkers need to be tested systematically."

The Early Detection Research Network Web site is http://edrn.nci.nih.gov/

The Clinical and Epidemiology Centers, their principal investigators, and funding amounts are: Elizabeth Unger, Centers for Disease Control and Prevention; Kathy Helzlsouer, Johns Hopkins University, $700,000; Alan Partin, Johns Hopkins University, $366,000; Dan Cramer, Brigham and Women's Hospital, $768,000; Dean Brenner, University of Michigan, $1,107,000; Henry Lynch, Creighton University, $525,000; William Rom, New York University School of Medicine, $1,068,000; Margaret Spitz, University of Texas M. D. Anderson Cancer Center, $838,000; Ian Thompson, University of Texas Health Sciences Center, $534,000.

The Biomarker Validation Laboratories principal investigators are: David Chia, University of California at Los Angeles, $296,000; William Grizzle, University of Alabama at Birmingham, $497,000; Peter Baker, National Institutes of Standards and Technology.

Data Management and Coordination Center principal investigators are: Ziding Feng, Fred Hutchinson Cancer Research Center, $662,000.

Funding Opportunities:

Program Announcements

PA PAR-00-102: Planning Grants: National Programs of Excellence in Biomedical Computing

Letter of Intent Receipt Date: Feb. 27, June 27, Oct. 27 annually; Application Receipt Date: March 27, July 27, Nov. 27 annually

Participating Institutes and Centers of NIH invite applications for P20 planning grants to establish the National Programs of Excellence in Biomedical Computing. The NPEBCs would speed the progress of biomedical research through the power of computing primarily in areas concerning management and analysis of data and modeling biological processes. As defined here, biomedical computing or biomedical information science and technology includes database design, graphical interfaces, querying approaches, data retrieval, data visualization and manipulation, data integration through the development of integrated analytical tools, synthesis, data archiving, data exchange, tools for electronic collaboration, and computational research including the development of structural, functional, integrative, and analytical models and simulations.

Inquiries: Richard Swaja, Office of Extramural Research, 1 Center Dr, Rm 152, Bethesda, MD 20892-0152, phone 301-402-2725; fax 301-496-0232; e-mail swajad@od.nih.gov

PA-00-099: Integrative and Collaborative Approaches to Research

This PA facilitates collaborative and interdisciplinary approaches to significant biological problems by investigators at different institutions. The initiative will use the R24 grant mechanism designed for groups of currently funded investigators working on a common problem, to 1) attract and coordinate expertise in different disciplines and approaches and 2) to provide access to specialized resources and equipment. The mechanism must involve investigators at different institutions and must introduce new collaborative and interactive activities that will further the shared research goals and significantly enhance what could be accomplished with the individual investigators' grant support.

Inquiries: James Cassatt, Division of Cell Biology and Biophysics, National Institute of General Medical Sciences, Bldg. 45, Rm 2AS19, Bethesda, MD 20892-6200, phone 301-594-0828; fax 301-480-2004; e-mail cassattj@nigms.nih.gov or Judith Greenberg, Division of Genetics and Developmental Biology, NIGMS, Building 45, Rm 2AS25, Bethesda, MD 20892-6200, phone 301-594-0943; fax 301-480-2228; e-mail greenbej@nigms.nih.gov

RFA Available

RFA NR-01-001: Nursing Research Exploratory Center Grants

Letter of Intent Receipt Date: Oct. 9, 2000

Application Receipt Date: Nov. 14, 2000

National Institute of Nursing Research invites applications for exploratory center grants in key clinical and basic areas of nursing research that establish a scientific basis for the care of individuals across the life span. NINR seeks to increase the numbers of research-intensive schools of nursing through the Nursing Research Exploratory Center grants P20s.

Inquiries: Carole Hudgings, chief, Office of Extramural Programs, National Institute of Nursing Research, Bldg. 45, Rm 3AN-12 MSC 6300, Bethesda, MD 20892-6300, phone 301-594-5976; fax 301-480-8260; e-mail carole_hudgings@nih.gov

Notice: Pre-Application Meeting for the Cooperative Human Tissue Network RFA-CA-01-009

The Resources Development Branch of the Cancer Diagnosis Program, Division of Cancer Treatment and Diagnosis, will hold a pre-application informational meeting on June 9, from 1-5 p.m. in Conference Room A, Natcher Building 45, NIH, Bethesda MD for investigators planning to submit applications in response to RFA-CA 01-009.

The complete text of the RFA is available at http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-01-009.html.

Potential applicants are not required to attend the pre-application meeting. A written transcript of the meeting

will be posted at http://www-cdp.ims.nci.nih.gov/ after the meeting.

Inquiries: Marianna Bledsoe, RDB, Cancer Diagnosis Program, DCTD, NCI, phone 301-496-7147; fax 301-402-7819; e-mail: mb80s@nih.gov.

In Brief:

ASCO Foundation Raised $200,000 In Its First Year

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Cancer Research Center, received the Herbert J. Block Memorial Lectureship Award for Distinguished Achievement in Cancer from the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute of Ohio State University. Potter, a member of the Hutchinson Center Public Health Sciences Division and a professor of epidemiology at the University of Washington School of Public Health and Community Medicine, was recognized for his contributions to cancer epidemiology, cancer prevention and the use of molecular methods in epidemiology. . . . **AMERICAN SOCIETY FOR CLINICAL ONCOLOGY FOUNDATION,** a not-for-profit charitable trust through which the society develops its fellowship programs, raised $200,000 in its first year to advance careers in clinical cancer research and to communicate cancer advances to oncologists. . . . **PATRICK WHITE**, director of public affairs for the American Association of Immunologists, was appointed director of legislative relations for the Federation of American Experimental Biology. White served many years on Capitol Hill and was the principle aide for legislative activities and external affairs for President George Bush science advisor, D. Allan Bromley. . . . **CANCER RESEARCH FUND** of the Damon-Runyon-Walter Winchell Foundation received $15 million from the Elli Lilly & Company to create the Clinical Investigator Award, a trainee and mentor program designed to reverse a 15-year field decline by recruiting new physicians into clinical research. The program will award five young physicians and their research mentors $1.2 million each year over five years for resources and training. In recognition that debt is one of the major stumbling blocks to clinical research recruitment, the Fund will retire up to $100,000 of any medical school debt upon successful completion of the program. **Richard O'Reilly**, chairman of the Department of Pediatrics and chief of the Marrow Transplantation Service at Memorial Sloan-Kettering Cancer Center, will be the program chairman. "Through our support of their mentors, we also wish to encourage university centers and leaders in clinical research to develop programs which nurture outstanding physician-scientists committed to patient-based investigations of human cancer," said O'Reilly. The following physician-scientists and their mentors are grant recipients: Rafael Fonseca and Philip Greipp, Mayo Clinic; Maura Gillison and Keerti Shah, Johns Hopkins University School of Medicine; Vered Stearns and Daniel Hayes, Georgetown University Medical Center; Robert Vonderheide and Lee Nadler, Dana-Farber Cancer Institute; Edus Warren and Stanley Riddell, Fred Hutchinson Cancer Research Center. . . . **CAROLYN ALDIGE**, president and founder of the Cancer Research Foundation of America and president of the National Coalition for Cancer Research, received the Howard University Hospital 2000 Legacy of Leadership Award for Distinguished Health Care Educator for her public education in advancing women's health issues through research and public policy. The award is given for excellence in service and leadership in the health care industry. . . . **JOINT ECONOMIC COMMITTEE,** headed by **Sen. Connie Mack** (R-FL), released "The Benefits of Medical Research and the Role of the NIH," a study that examines the positive impact of NIH funded medical research. According to the study, the NIH budget, currently $16 million per year, is about one-half of one percent of the $3 trillion costs of disease in the U.S. annually. The value of life gains in health improvements through medical research represents $2.4 trillion a year. Each $1 invested in NIH yields a return of $15 if NIH is responsible for just 10 percent of these gains, the study said. NIH-funded research was involved in developing seven of the 21 most important drugs from 1965 to 1992, the study said. The JEC report is available at http://www.jec.senate.gov. . . . **SEYMOUR PERRY**, a former deputy director of the NCI Division of Cancer Treatment, former director of the NIH Office of Medical Application of Research, and former professor and chairman in the Georgetown University Medical School, died of prostate cancer May 20 at his home in Washington, DC. He was 78. Since 1995, Perry had been director of the World Health Organization Collaborating Center for Health Technology Assessment, where he established a network of 650 health care professionals around the world researching the safety, efficacy, and cost of medical technologies.

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Business & Regulatory Report

Formerly "Cancer Economics"

Product Approvals & Applications:

FDA Approves Mylotarg For First Relapse Of Acute Myeloid Leukemia In Patients 60+

American Home Products Corp. (NYSE:AHP) said it had received FDA approval for Mylotarg (gemtuzumab ozogamicin for injection), the first targeted chemotherapy agent using monoclonal antibody technology for the treatment of patients 60 years and older in first relapse with CD33-positive acute myeloid leukemia that are not considered candidates for cytotoxic chemotherapy.

The safety and efficacy of Mylotarg in AML patients with poor performance status and organ dysfunction has not been established, the company said.

In three multi-national phase II trials, involving 142 patients, Mylotarg

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Research Funding:

Pharmacia Corp. Forms $1 Million Fund To Support Anthracycline Research

Pharmacia Corp. (NYSE: PHA) of Peapack, NJ, said it has established a $1 million Ellence Research Fund to support the advancement of anthracycline research.

Ellence (epirubicin hydrochloride injection) was approved by FDA in September 1999, as a component of adjuvant therapy in the treatment of node positive early breast cancer following surgery.

In an announcement that coincided with the annual meeting of the American Society of Clinical Oncology, the company said developmental, clinical, nursing, pharmacoeconomic, and pharmacologic research will be eligible for funding. A panel of clinical and research experts in breast cancer will select projects based on their originality, the company said.

The deadline for proposal submission will be Aug. 15. Recipients will be announced in October, the company said.

Formation of the fund is the first major announcement of the newly established Pharmacia Oncology Franchise, which will bring together the company's oncology research and marketing resources.

The drug figured in nearly 100 abstracts at the ASCO meeting. Introduced in 1982, Ellence has been available in more than 80 countries. The drug is marketed as Farmorubicin outside the U.S.

For further information on the Ellence Research Fund, call 908-901-8623.

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

FDA Approves Mylotarg For AML; Marketed By Wyeth

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as a single agent produced a 26 percent overall remission rate in patients 60 and older with CD33-positive AML in first relapse. Median duration of overall survival for the 142 patients was 5.9 months. A 4 percent incidence of severe mucositis was observed with the treatment, the company said.

Wyeth-Ayerst Laboratories, a pharmaceutical division of AHP, will marked the agent, the company said.

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Biomira Inc. (Nasdaq: BIOM) (TSE: BRA) of Edmonton, said FDA has given Fast-Track designation to Theratope, as an adjunct to the first line combination chemotherapy for metastatic breast cancer.

Earlier studies have suggested the vaccine offers significant survival benefits over standard treatment alone, the company said. In one arm of two parallel prospectively randomized trials, Theratope vaccine-treated patients had a median survival of 26.5 months compared to 9.2 months in a retrospective control group. Biomira said it is currently evaluating the vaccine in a phase III trial with 900 evaluable patients and expects to complete enrolment by the end of this year.

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Cell Therapeutics Inc. (Nasdaq:CTIC) of Seattle, said FDA has granted priority review and has accepted for filing its new drug application for Arsenic TriOxide, a drug treatment for relapsed or refractory acute promyelocytic leukemia.

The company said NCI is conducting 13 clinical trials evaluating the safety and efficacy of ATO in ten different cancer indications. ATO recently received orphan drug designation for the treatment of multiple myeloma, the company said.

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Sicor Inc. (Nasdaq: SCRI) of Irvine, CA, said its subsidiary, **Gensia Sicor Pharmaceuticals Inc.**, has received abbreviated new drug application approval from FDA for Cisplatin Injection in established combination therapy with other approved chemotherapeutic agents for metastatic testicular and ovarian tumors.

The approval marks the sixth ANDA approval Gensia Sicor Pharmaceuticals has received this year, the company said. According to IMS, a market research firm, U.S. sales of Cisplatin, marketed by Bristol Myers Squibb Co., were approximately $100 million in 1999.

In addition to cisplatin, SICOR supplies doxorubicin, etoposide, daunorubicin and vincristine in polymer plastic vials.

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Varian Medical Systems Inc. (NYSE:VAR) of Palo Alto, CA, said it received 510K clearance from FDA to market its image-based 3D BrachyVision 6.0 treatment planning software.

The BrachyVision 6.0 software is a full function planning system for all brachytherapy treatments, the company said. The software is used to develop plans for low dose rate brachytherapy as well as temporary implants of radiation sources for high dose rate brachytherapy. It is intended for rapid generation of optimal treatment plans using innovative 3-D images that enable doctors to more easily view the tumor, surrounding anatomy, and their relationship with varying radiation doses, the company said.

With 3D image-based planning capabilities, the software enables clinicians to view treatment areas from all angles. Tumors, surrounding anatomical structures, and varying radiation dose levels can be easily distinguished and viewed using contrasting colors. The software provides planners with a unique interactive Dose Shaper that allows the physician to interactively shape the dose distribution to conform more precisely to patient anatomy, the company said.

"With this new tool, it's possible to develop more sophisticated plans in less than half the time that is required with conventional 2D planning methods and tools," said William Hyatt, general manager of Varian Medical Systems. "Treatment plans can be completed in as little as 10 minutes for simple cervix cases and in an hour or less for more complex cases."

Oncology Management:

One Health Plan, Genzyme Agree On Genetic Testing

One Health Plan Inc. of Denver, said it has signed an agreement with **Genzyme Genetics** to give its 3.5 million members nationwide access to the Genzyme Genetics prenatal biochemistry, pre- and post-natal cytogenetics, molecular genetics and cancer genetics testing and genetic counseling services.

The new services would improve the ability of OHP members to make informed decisions regarding their healthcare," said Donna Goldin, executive vice president and CEO for the One Health Plan companies. "Genzyme Genetics is the largest provider of genetic testing and counseling services in the world and has a record of providing the highest quality services," Goldin said.

One Health Plan is a subsidiary of Great-West Life & Annuity Insurance Co.

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U.S. Oncology Inc. (Nasdaq: USON) of Houston, **CTI Inc.** of Knoxville, and **PETNet Inc.** of Hoffman Estates, IL, said they have entered into an agreement to make Positron Emission Tomography part of the U.S. Oncology cancer detection, diagnosis, and treatment protocols.

CTI said it would provide the U.S. Oncology network with 30 PET scanners during the next year. PETNet would become the exclusive provider of PET radiopharmaceuticals, the company said.

Clinical Trials:

ECOG To Cease Participation In Melanoma Vaccine Study

Progenics Pharmaceuticals Inc. (Nasdaq: PGNX) of Tarrytown, NY, said the Eastern Cooperative Oncology Group would conclude its participation in the phase III trial for the GMK melanoma vaccine.

The company said it plans to continue the trial as an extension study until the scheduled completion of the original trial.

The decision was made after ECOG performed an unplanned early analysis on a subset of the 880 patients enrolled in the trial, the company said. Although the trial is fully enrolled, the analysis was conducted at a time when only about half of the patients had received the two years of GMK therapy provided in the study protocol and most of the interferon patients had completed their full course of therapy, the company said.

ECOG informed Progenics that the interim analysis indicated the relapse-free and overall survival rates for patients receiving the vaccine were lower than those for patients receiving high-dose alpha-interferon, an approved agent with a well-documented early onset of clinical effect, the company said. As expected, GMK was better tolerated than alpha-interferon with about five times less frequent and much less severe side effects, the company said.

"The onset of clinical effect for a vaccine appears later than that of other cancer therapies which are given in high doses over a much shorter period of time," said Alan Houghton, chairman of the Progenics Cancer Scientific Advisory Board, chairman, Immunology Program at Memorial Sloan-Kettering Cancer Center and professor, Cornell University Medical Center. "From what we know, the relapse-free and overall survival rates for the GMK vaccine in the phase III trial are tracking generally as expected at this time based on our previous clinical experience."

"ECOG has been indispensable in its ability to enroll 880 melanoma patients over a relatively short period," said Paul Maddon, chairman and CEO of Progenics "With full accrual, ECOG has substantially completed its contribution to the trial. We believe that in the longer term, the benefits of this innovative therapy to melanoma patients can be demonstrated."

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Abbott Laboratories (NYSE: ABT) of Abbott Park, IL, said it is collaborating with **Antisoma**, a UK-based biopharmaceutical company of tumor targeting products, to co-develop HMFG1 (Human Milk Fat Globule 1) for the adjuvant treatment of ovarian cancer.

The company said recently diagnosed ovarian cancer patients are needed at medical sites across the country for a phase III trial of a new single injection therapy. Patients recently diagnosed with ovarian cancer in stage Ic disease and patients

currently receiving chemotherapy may be eligible for the trial, the company said. Additional information is available from the sponsors, tel.:800-266-6644.

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IntraBiotics Pharmaceuticals Inc. (Nasdaq: IBPI) of Mountain View, CA, said it has begun a phase III trial of Protegrin IB-367 Rinse for oral mucositis resulting from radiationtherapy and chemotherapy.

The study will enroll 316 patients at approximately 20 sites in the U.S. and Europe, the company said.

"Oral mucositis arguably represents one of the biggest hurdles that continue to plague our treatment of cancer patients and its successful management is vital to improvements in patient care," said Roy Beveridge, director of Stem Cell Transplant at Inova Fairfax Hospital in Fairfax, VA, and a company investigator.

Henry Fuchs, vice president of clinical affairs at IntraBiotics, said another study will evaluate patients with head and neck cancer who are undergoing radiation therapy.

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Onyvax Ltd., a London-based private cancer vaccine development company said clinical trials would begin on two of its vaccines for colorectal cancer.

The first trial, conducted by Fiona Lofts, consultant oncologist at St. George's Hospital, London, will recruit 45 patients who will be treated with an Onyvax cell-based vaccine and with an antibody-based vaccine licensed from the Cancer Research Campaign.

The second trial, conducted by Mukul Dube at the Queen's Medical Centre, Nottingham, will recruit a further 45 patients scheduled for primary surgery and then treated with an antibody- based vaccine.

"Clinical experience to date with our prostate cancer vaccine has shown an excellent safety and side- effect profile together with potent immune responses induced by the vaccine," said Angus Dalgleish, research director. Patient recruitment information is available on the Colorectal Cancer Vaccine Trial Helpline: +44 (0)20 8682 9131.

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SafeScience Inc. (Nasdaq: SAFS) of Boston, said it has it has received written notice of full approval from the Western Institutional Review Board for a phase II, open label, safety, efficacy, and pharmacokinetic study of GBC-590 in patients with refractory or relapsing carcinoma of the pancreas who have failed one prior regimen of chemotherapy. Corliss Newman, Senior Instructor of Oncology of the University of Rochester Cancer Center is the principal investigator for the study.

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SuperGen Inc. (Nasdaq: SUPG, SUPGW & SUPGZ) of San Ramon, CA, said it has been awarded a grant of $750,000 by NCI to initiate clinical trials of IPdR (5-iodo-pyrimidinone-2'-deoxyribose) as an oral radiation- sensitizing drug for radiation-resistant cancers.

Following oral administration, IPdR is converted by aldehyde oxidase into IUdR within the liver and is then released into the blood stream. IUdR has been under investigation by NCI as a potential agent to sensitize cancer cells to radiation, and has been studied in humans for a number of years, the company said.

However, IUdR is available only in intravenous form and is toxic to the bone marrow and gastrointestinal system. The SuperGen IPdR compound, a prodrug of IUdR, is orally active, and preclinical studies have shown that by administering IPdR orally, the same radiation-sensitizing effects can be achieved as with IUdR, but with less toxicity, the company said.

"This drug has the potential to benefit most patients who receive radiation therapy for cancer," said Timothy Kinsella, chairman, Radiation Oncology at Case Western and lead investigator of the single- and multi- dose trial.

* * *

Vion Pharmaceuticals Inc. (Nasdaq: VION) of New Haven, CT, said it has initiated an additional phase I study of Triapine, a ribonucleotide reductase inhibitor, for solid tumors and acute myelogenous leukemia.

The trial, which will test the agent in a 96-hour continuous infusion study, will be conducted at the Albert Einstein College of Medicine/Montefiore Medical Center, under the direction of Scott Wadler and Della Makower, the company said.

Vion said data from an earlier phase I single dose study of Triapine demonstrated its safety profile and ability to reach pharmacologically relevant serum concentrations. The current trial, and an ongoing study of short infusions administered daily for 5 days, will continue to evaluate the safety profile and feasibility of extending injections over several days, which, in preclinical animal tumor models, demonstrated

Triapine's greatest antitumor activity, the company said.

In preclinical studies, Triapine exhibited significant in vitro and in vivo activity against human ovarian cancer grafted onto mice and in mouse tumors for leukemia and lung cancer, the company said. "The data suggest that riapine could be combined successfully with many of the standard cancer treatment regimens, and thus, will have broad clinical utility," said Alan Kessman, president and CEO of Vion.

Deals & Collaborations:

Vysis, Genentech In Agreement On HER-2 Breast Cancer Test

Vysis Inc. (Nasdaq: VYSI) of Downers Grove, IL, a developer and marketer of clinical products providing information for genomic disease management, said it has signed a collaborative agreement with **Genentech Inc.** (NYSE: DNA) of South San Francisco, to extend the use of Vysis' FDA approved PathVysion HER-2 breast cancer test kit as an aid in the assessment of patients for whom Herceptin treatment is being considered.

Genentech is the developer and marketer of the Herceptin (trastuzumab) monoclonal antibody treatment for metastatic breast cancer.

The collaboration will also extend to future clinical studies in other cancers for the potential assessment of patients for whom Herceptin treatment may be considered where there is evidence of HER-2 amplification, the company said.

The Vysis PathVysion assay is based on the company's proprietary FISH (fluorescence in situ hybridization) DNA probe technology.

"Herceptin is a breakthrough cancer therapy and the first in an expected wave of therapies that are selected for use based upon the individual patient's genetic profile, in this case the amplification status of the HER-2 gene," said Dennis Slamon, chief of the Division of Hematology and Oncology, and director of clinical research at Jonson Comprehensive Cancer Center.

"I believe the Vysis PathVysion test is the most accurate and reliable means of determining patient HER-2 status," said Slamon, who identified the association between the HER-2 gene and aggressive breast cancer.

The PathVysion assay is approved by the FDA to detect HER-2/neu gene amplification and is intended as an adjunct to existing clinical and pathologic information used as prognostic factors in node positive, stage II breast cancer.

In addition, the assay is an aid in predicting survival of these patients treated with CAF, the company said. Vysis said that under collaboration it will seek to obtain labeling claims for breast cancer and additional cancers for which Herceptin treatment is currently under development.

"We expect to make a coordinated FDA submission with Genentech in the near future," said John Bishop, Vysis president & CEO.

In related developments:

—At the ASCO meeting, Robert Mass, a clinical scientist at Genentech, presented data on the clinical outcome benefit of Herceptin therapy based upon measurement of HER-2 gene amplification by the PathVysion FISH test.

—**ChromaVision Medical Systems Inc.** (Nasdaq: CVSN) of San Juan Capistrano, CA, manufacturer of the Automated Cellular Imaging System, presented data on the value of ACIS in HER2 assessment.

The data resulted from a collaborative study with NIH, the Institute of Pathology in Basel, and two diagnostic companies, DAKO A/S and Vysis Inc., the ChromaVision said in a press release.

"Perhaps the most striking observation is the finding that ACIS scoring allowed for the identification of prognostically distinct patient populations which could not be identified by alternative analytical methods evaluated in the study," said Kenneth Bauer, ChromaVision's Chief Science Officer. "Additional ChromaVision data obtained in studies of over 1,500 patients indicate considerable potential for the highly accurate and quantitative scoring of HER2 expression relative to the current subjective manual method which leads to poor inter-laboratory reproducibility."

The abstract is titled "Automated, High-Throughput Tissue Microarray Analysis for Assessing the Significance of HER2 Involvement in Breast Cancer."

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Vertex Pharmaceuticals Inc. (Nasdaq: VRTX) of Cambridge, MA, and **Novartis Pharma AG** of Basel, Switzerland, said they have entered into an alliance to discover, develop, and commercialize small molecule drugs directed at targets in the kinase protein family.

Novartis said the collaboration could make pre-

commercial payments to Vertex of $800 million, based on the successful discovery and full development of eight compounds.

The alliance creates a new operating model for pharmaceutical research and development, combining Vertex's integrated parallel drug discovery approach in target families with the Novartis portfolio management system, with its emphasis on optimizing the early development phase of new compounds and promotion of selected compounds to rapid clinical development. This is the pharmaceutical industry's most significant alliance to date in the discovery of new drugs based on targets uncovered by genomic and proteomic research.

Novartis said it would provide Vertex with a $15 million initial payment and further research funding of $200 million over 6 years, and Vertex will have responsibility for drug discovery and clinical proof-of-concept testing of drug candidates. Novartis said it would have exclusive worldwide development, manufacturing and marketing rights to eight clinically and commercially relevant drug candidates that it accepts for development from Vertex.

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ADAC Laboratories (Nasdaq:ADAC) of Milpitas, CA, and **American Diagnostic Medicine** of Elmhurst, IL, said they have signed an exclusive agreement with **International Oncology Network** of Baltimore, MD, a physician-driven provider network specializing in oncology, to offer PET imaging capabilities to the ION network of 2,000 oncologists.

The agreement is an offshoot of FirstNuclear, a joint venture between ADAC and ADM, to create nationwide freestanding PET centers and total turnkey solutions for in-house PET testing, the companies said. The program provides a trained technologist to perform the diagnostic exams, all supplies, marketing support, health physics, state licensing and procedures coding. It also includes a network of leading PET specialists to provide over-read capabilities and educational opportunities for radiologists at each PET center, the companies said.

"Under the agreement, any ION member may contract with FirstNuclear to bring this technology into their offices as they work to provide their patients with early diagnosis and the most beneficial cancer treatments," said Ron Conheim, senior vice president of ION.

The U.S. Health Care Financing Administration has approved Medicare reimbursement for PET scans in lung cancer detection and staging, colorectal cancer, Hodgkin's and non-Hodgkin's lymphomas, and melanoma. Breast, head-and-neck and other cancers are under HCFA consideration for approval, the companies said.

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Axcan Pharma Inc. of Mont Saint-Hilaire, Quebec, said it has signed an agreement with **QLT PhotoTherapeutics Inc.** of Vancouver, to acquire worldwide rights to Photofrin, a photodynamic cancer drug therapy.

Photofrin is injected intravenously and selectively accumulates in tumor cells, the company said. Activation of the drug by a non-thermal laser light at the tumor site produces a toxic form of oxygen that then destroys the cancer cells. Unlike surgery and radiation, the drug therapy entails a low risk of damage to adjacent healthy tissue, allowing for other treatments, if needed, company said.

In another development, QLT and Axcan said they will complete the ongoing clinical trial program for the treatment of high grade dysplasia associated with Barrett's esophagus.

Studies to date indicate that the incidence of Barrett's esophagus is increasing steadily, particularly among middle-aged males with stressful lifestyles and a mid to high socio-economic status, the companies said.

Under the stock subscription agreement, QLT said it will pay CDN $19,250,000, or CDN $15.00 per share, for 1,283,333 shares of Axcan common stock. Under the asset purchase agreement QLT said it will sell, license or sub-license to Axcan all its rights, title and interest in Photofrin, including the sale the QLT European subsidiary which owns the European registrations for Photofrin. In exchange, Axcan said it will pay QLT CDN $39.25 million.

Axcan said it will assume worldwide responsibility for the marketing efforts for Photofrin at closing, except for Japan where Wyeth-Ayerst Laboratories will continue to have the exclusive right to market and distribute the drug.

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Elan Corp. plc (NYSE: ELN) of Dublin, Ireland, said it has completed acquisition of the **Liposome Company Inc.** (Nasdaq: LIPO) of Princeton, NJ.

Liposome will operate as a separate business unit within Elan, the company said.

Under the agreement, Elan said it acquired all of the Liposome outstanding stock in a tax-free, stock-for-stock transaction. Liposome shareholders receive

0.3850 of an Elan ADS and one contingent value right for each share of Liposome common stock.

The agreement governing the contingent value rights will provide for a cash payment by Elan to holders of up to $98 million, with $54 million contingent on certain approvals of Myocet for marketing in the European Union, and $44 million contingent on Myocet reaching certain sales milestones outside the U.S. The first stage of approvals for the marketing of Myocet in the European Union has been received, the company said.

Elan said it would account for the transaction using the purchase method and will incur a one-time charge representing the write-off of acquired in-process research and development. Excluding the one-time charge, Elan expects the transaction to be neutral in 2000 and accretive in 2001 after cost synergies are included.

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Hyseq Inc. (Nasdaq: HYSQ) of Sunnyvale, CA, said it has entered into a two-year extension of its 1997 exclusive gene discovery collaboration with **Chiron Corp.** (Nasdaq: CHIR) of Emeryville, CA, to develop solid tumor cancer therapeutics, diagnostic molecules and vaccines.

During the initial three-year term of the collaboration, Hyseq said it processed over 8 million samples for Chiron, resulting in filings for patent applications relating to over 11,000 gene discoveries and identification of specific gene targets. Chiron said it would pursue potential product candidates based on the gene discoveries.

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ImmunoGen Inc. (Nasdaq: IMGN) of Cambridge, MA and **British Biotech plc** (LSE: BBG) of Cambridge, England, said they have entered into a licensing agreement to develop and commercialize huN901-DM1, the ImmunoGen tumor-activated prodrug, for treatment of small-cell lung cancer.

huN901-DM1 consists of a humanized monoclonal antibody targeting SCLC cells, coupled with, DM1, a cytotoxic agent derived from maytansine. In preclinical studies, ImmunoGen said huN901-DM1 eradicated SCLC tumors. In the same studies, cisplatin and etoposide, drugs used in current SCLC treatment, produced only temporary interruption of tumor growth, the company said.

British Biotech said it has been granted the exclusive right to develop and commercialize huN901-DM1 in the European Union and Japan. ImmunoGen said it retains the rights to commercialize huN901-DM1 in the U.S. and the rest of the world, as well as the right to manufacture the product worldwide. British Biotech said it paid an upfront fee of $1.5 million for its territorial rights.

Under the agreement, British Biotech said it is responsible for conducting the clinical trials necessary to achieve regulatory approval in the US, EU and Japan. ImmunoGen said it is responsible for the remaining preclinical development, and will be reimbursed for manufacturing the product for clinical trials. A phase I trial will start in the fourth quarter of this year, the company said.

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Medarex Inc. (Nasdaq: MEDX) of Princeton, NJ, said it has entered into an antibody development agreement with **Centocor Inc.**, a subsidiary of **Johnson & Johnson** (NYSE: JNJ).

The agreement allows Centocor and other affiliates of J & J to access the HuMAb-Mouse technology for an unlimited number of targets. Under the terms of the agreement, Medarex said it will receive technology access fees, and could also receive license fees, milestone fees and royalties on product sales.

Centocor has developed a high-affinity human antibody from the HuMAb-Mouse, which is in pre-clinical development, and has other product candidates as well, the company said.

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Protein Design Labs Inc. (Nasdaq: PDLI) of Fremont, CA, said it has entered into a licensing and joint development agreement with **Toagosei Co., Ltd.**, of Tokyo for SMART Anti-VEGF, an antibody that binds to vascular endothelial growth factor, for cancer treatment.

Under the agreement, PDL said it has obtained exclusive development and marketing rights to SMART Anti-VEGF in North America and the first option to obtain exclusive rights to market the antibody in Europe and other markets, except Japan. Toagosei has exclusive rights to market the antibody in Japan. PDL said it will direct the clinical development program, and the companies will share development costs and profits from sales of the antibody, if any, in markets outside Japan.

A phase I open-label, multicenter study clinical trial for relapsed or refractory solid tumors began in January under the auspices of the European Organization for Research and Treatment of Cancer.

An antibody to VEGF has already been reported

in phase II clinical trials to have potential for the treatment of metastatic colorectal and non-small cell lung cancer, said Daniel Levitt, president of research and development at PDL. In experiments conducted at Toagosei, SMART Anti-VEGF has shown potent activity in inhibiting the growth of a large number of highly diverse human tumors growing in nude mice. Levitt said that particularly encouraging results were obtained in combination with chemotherapy.

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Protarga Inc. of Conshohocken, PA, said it has entered into a cooperative research and development agreement with NCI to accelerate the development of novel anti-cancer therapies using the Protarga Targaceutical technology for drug targeting.

Under the agreement, NCI will supply novel anti-cancer agents to Protarga from its extensive compound library and Protarga will chemically link these agents to its fatty acid vectors, the company said. NCI will conduct preclinical studies on the resulting Targaceutical compounds to identify those suitable for clinical study. Protarga said it has the exclusive right to license patents resulting from the collaboration.

This is the first NCI drug development program to systematically apply fatty acid vector technology to anti-cancer agents, the company said. Fatty acid vectors may increase the quantity of drug that reaches the tumor cells, thereby increasing anti-cancer activity. At the same time, the amount taken up by healthy cells may be reduced, thereby reducing side effects. Edward Sausville, associate director, Developmental Therapeutics at NCI, is principal investigator for the CRADA.

Preclinical studies with the new class of Targaceutical drugs have demonstrated that more of the therapeutic agent may be delivered to diseased tissue if it is linked to an appropriate fatty acid vector, the company said.

Taxoprexin DHA-paclitaxel, the first Protarga Targaceutical drug for oncology, is being tested in a phase I study at Johns Hopkins Hospital with a variety of solid tumors.

* * *

SuperGen Inc. (Nasdaq: SUPG & SUPGZ) of San Ramon, CA, said it has entered into a cooperative research and development agreement with NCI for decitabine, its anticancer compound.

Under the agreement, SuperGen said it would provide decitabine to NCI for clinical studies in solid tumors and hematological malignancies.

The NCI-sponsored studies will also examine the decitabine mechanism of action—hypomethylation of DNA—in gene regulation and the regulation of growth and redifferentiation of malignant cells, the company said.

"While NCI engages in a vigorous exploratory program designed to identify anticancer activity in a number of indications, SuperGen will continue to move decitabine into phase III studies for MDS and phase II studies for non-small cell lung cancer," said Joseph Rubinfeld, chairman and CEO of SuperGen.

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Vion Pharmaceuticals Inc. (Nasdaq: VION) of New Haven, CT, said it has initiated an additional phase I study of Triapine, a ribonucleotide reductase inhibitor, for solid tumors and acute myelogenous leukemia.

The trial will be conducted at the Albert Einstein College of Medicine/Montefiore Medical Center under the direction of Scott Wadler and Della Makower.

In preclinical studies, Triapine exhibited significant in vitro and in vivo activity against human ovarian cancer grafted onto mice and in mouse tumors for leukemia and lung cancer, the company said.

Patents:

Myriad Wins Patent For p10 Tumor Suppressor Gene

Myriad Genetics Inc. (Nasdaq: MYGN) of Salt Lake City, said it has been awarded patent number 6,060,301 by the U.S. Patent and Trademark Office for the p10 gene.

The gene, which may provide the basis for the development of products to diagnose and treat many common cancers, is a tumor suppressor that has been found to mutate in melanoma, leukemia, lymphoma and prostate cancer, colon cancer, breast cancer, kidney cancer, pancreatic cancer, bladder cancer, stomach cancer, ovarian cancer, uterine cancer and testicular cancer, the company said.

"Myriad continues to build an extremely strong intellectual property position through the award of patents on full length genes with known function and disease association intact," said Peter Meldrum, president and CEO of Myriad Genetics Inc. "The company believes that its patents are the strongest form of patent protection available for genomic discoveries."

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