THE CANCER LETTER INTERACTIVE

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

Vol. 27 No. 39
Oct. 26, 2001

House Approves NCI's First $4 Billion Budget, $22.8 Billion For NIH In FY2002

The House Appropriations Committee called funding for NIH one of its "very highest priorities" in a report accompanying the fiscal 2002 funding bill for the Departments of Labor, HHS, and Education.

The House passed the bill on Oct. 11, providing $22.87 billion for NIH, $2.579 billion above last year's appropriation.

The report also:

—Includes $4.146 billion for NCI, $409 million more than last year.

—Includes $393.3 million for countering bioterrorism. An estimated $92.7 million will be used to fund research supported by NIH.

—Provides $4.308 billion for the Centers for Disease Control and Prevention, $264.2 million above last year's funding level.

—Contains the same language included for the past several years to prohibit the use of funds for research involving human embryos. This language also has the effect of prohibiting Federal support for human cloning.

(Continued to page 2)

In Brief:

Foundation Honors Three In Oncology; Society Wins Software Grant From Microsoft

AMERICAN-ITALIAN CANCER FOUNDATION will honor three individuals at its 20th anniversary benefit gala Nov. 12, in New York. The Life Achievement Award will go to **Umberto Veronesi**, scientific director of the European Institute of Oncology, founder of the European School of Oncology and former minister of health of Italy; the Scientific Excellence in Medicine Awards will be presented to **Maurizio Ponz de Leon**, professor of internal medicine, University of Modena and to **Bernard Levin**, vice president, Cancer Prevention, M.D. Anderson Cancer Center. . . . **LEUKEMIA & LYMPHOMA SOCIETY** received $1.25 million grant from the 2001 Microsoft Technology Leadership Grant Program. The annual grant provides software donations to large, national non-profit organizations that are able to expand their use of information technology to support their mission. The two-year donation package includes Windows 2000, Office XP, Exchange 2000 and Visio and Visual Basic programming tools. Created in 1983, the Microsoft Giving Program increases access to technology for disadvantaged communities and supports community organizations in education, human services, civic development, the arts

(Continued to page 8)

In Congress:
House Report Calls NIH Funding High Priority
. . . Page 2

House Committee Identifies Blood Cancers, Metastasis, Ovarian, Prostate Cancers Among Areas Needing More Research Funds
. . . Page 3

CDC Urged To Enhance Public Education About Lymphoma, Orphan Cancers
. . . Page 7

House Report Calls NIH Funding High Priority

(Continued from page 1)

The report is available at ftp://ftp.loc.gov/pub/thomas/cp107/hr229.txt

Excerpts of the report follow:

National Institutes Of Health

The Committee provides $22,874,971,000, for the 26 appropriations, which together fund the programs of NIH. The total in the bill is $2,579,711,000 above the fiscal year 2001 comparable level and the same as the budget program request. This funding level provides a 12.3 percent increase in total for the research components of NIH, the same as the budget program request. The funding levels provided in the bill for each of the Institutes and Centers reflect the same program level as the Administration request. The budget proposed to increase the Public Health Service evaluation tap from one percent to two percent. The Committee has not agreed to this proposal. The Committee has adjusted the appropriation for each Institute and Center based on a one percent evaluation tap amount and provides each Institute and Center with the same program level as requested by the President. Within the funds provided, the Committee assumes a 4.6 percent pay increase.

Committee Priorities—The Committee views NIH as one of its very highest priorities and has made difficult resource allocation decisions throughout the bill to provide what it believes is the necessary funding level for NIH. NIH is the world's leading biomedical research institution; its investments in research save lives, relieves suffering, and reduce health care costs while creating jobs and economic growth in a global economy. This research has produced major advances in the treatment of cancer, heart disease, diabetes, and mental illness that have helped thousands of American families. The U.S.'s ability to translate scientific discoveries into new product development has resulted in its lead over Europe and Japan in pharmaceutical and biotechnology patents. While the Committee is firm in its commitment to budget restraints, it believes that funding of biomedical research is an important investment in the future health and economic well-being of our nation.

Balance in the Research Portfolio—The Committee believes that NIH should distribute funding on the basis of scientific opportunity. As a result, the Committee has allocated the Institute appropriations consistent with the distribution recommended by NIH and reflecting the Director's judgment of scientific opportunity. The Committee urges the Director and the Administration to continue to resist pressures to earmark, set-aside and otherwise politicize these invaluable resources. If NIH believes that adjustments to this allocation are necessary as the fiscal year 2002 appropriations bill moves through the legislative cycle, the Committee would be pleased to consider them in later action on the bill.

To enhance NIH's flexibility to allocate funding based on scientific opportunity, the Committee has attempted to minimize the amount of direction provided in the report accompanying the bill. For example, there are no directives to fund particular research mechanisms, such as centers or requests for applications, or specific amounts of funding for particular diseases.

In stating that scientific opportunity should be the basis for allocating research funding, the Committee understands that other factors also are relevant to NIH's decisions, including such considerations as the infectious nature of a disease, the number of cases and deaths associated with a particular disease, the Federal and other costs of treating a disease, the years of productive life lost due to a particular disease, and the estimated proximity to research breakthroughs. The Committee does not presume to judge which criteria should take precedence

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

World Wide Web: http://www.cancerletter.com

Editor & Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
E-mail: news@cancerletter.com

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
E-mail: info@cancerletter.com

Subscription $295 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd

or carry the greatest weight in individual funding decisions, but urges NIH to consider the full array of relevant criteria as it constructs its research portfolio.

AIDS Funding—Consistent with the philosophy outlined above, the Committee has chosen not to earmark a specific dollar amount for AIDS research. The Committee understands that it would be NIH's intent to allocate AIDS funding consistent with the Director's recommendations. The Committee intends that the funds allocated for AIDS should be spent in a manner fully consistent with the AIDS research plan developed by the Office of AIDS Research and expects the Director of NIH to use the full authority of his office to ensure that this occurs. The Committee has provided the Director of OAR, jointly with the Director of NIH, transfer authority to reallocate up to three percent of funds designated for AIDS research among Institutes, subject to normal reprogramming procedures. The Committee encourages NIH to use this authority whenever it believes that an adjustment in the allocation of AIDS funding between Institutes is appropriate to achieve scientific objectives or to facilitate promising research efforts.

The Committee has provided funding for the OAR within the Office of the Director and intends that the OAR will maintain its current structure and responsibilities, including the allocation of an emergency discretionary fund.

Government Performance and Results Act—The Committee recognizes that the development of programmatic indicators for NIH under the Government Performance and Results Act is one of the most difficult conceptual and methodological problems in the Act's implementation. NIH should continue to work with the National Academy of Sciences and the other science agencies to develop a better conceptual and theoretical framework for such measures. The Committee believes that NIH should begin to implement the Act where it can. Measures of administrative efficiency and effectiveness can and should be adopted and tracked. Similarly, indicators of the ability of systems to support the research enterprise exist, and should be included. Presentation of these measures, including goals for improvements, baselines and reporting systems are an initial step. Information presented with the President's budget should include improvements in these indicators resulting from proposed funding levels. In addition, the Committee will expect the Director to include a report in the fiscal year 2003 appropriations budget justifications on the progress toward indicators relating directly to research and the translation of basic research findings to medical and other applications.

National Cancer Institute

The Committee provides $4,146,291,000 for NCI, which is $409,074,000 above the fiscal year 2001 comparable level and the same as the budget program request.

Blood Cancers—The Committee is pleased that NCI has conducted a progress review group on lymphoma, leukemia and myeloma to evaluate opportunities for research in these areas and looks forward to receiving a copy of the final report. The Committee requests that the Director of the Institute be prepared to provide a progress report on lymphoma and hematological cancer research, including a proposed budget plan, at the fiscal year 2003 appropriations hearing.

The Committee urges NCI to enhance research support to improve the understanding of, and develop treatments for, myelodysplasia, a serious blood disorder affecting primarily older Americans and individuals who have previously undergone radiation or chemotherapy treatment for cancer.

Bone Disease—The Committee encourages NCI to include multiple myeloma, a cancer of the plasma cells of the bone marrow, in its study of bone involvement in certain cancers. The Committee urges NCI to collaborate with NIAMS in translational research activities to capitalize on recent advances in the study of biophosphonates, a class of drugs that strengthen bone through all available mechanisms, as appropriate.

Cancer Metastases—The Committee encourages NCI to conduct research to develop a better understanding of the unique role bone microenvironment plays in cancer metastatic to bone, in particular, in breast cancer, prostate cancer and myeloma through all available mechanisms, as appropriate, including the development of animal models of bone metastases and the identification of novel therapeutic targets and modalities to prevent and treat bone metastases.

Chronic Lymphocytic Leukemia—Chronic Lymphocytic Leukemia, the most common form of adult leukemia in the U.S., is characterized by an accumulation of abnormal lymphocytes in the blood and bone marrow. The Committee understands that NCI awarded a program project grant last year to establish and lead a multi-disciplinary national research consortium to study CLL at both the cellular and

clinical levels. The Committee encourages NCI to consider expanding the scope of research activities of the consortium through all available mechanisms, as appropriate.

Five a Day Nutrition Program—The Committee commends the NCI's national 5 A-Day program and encourages the Institute to conduct research on how best to promote healthy eating, especially fruit and vegetable consumption. This research should include, but not be limited to, research on children and adolescents, the general adult population, low-income and disparate groups, especially African Americans and Latinos and ways to transfer already-developed technologies to other government agencies and to non-profit, civic, and other organizations.

Lymphoma—The incidence of non-Hodgkin's lymphoma has grown by an estimated 80 percent between 1973 and 1997 and has a survival rate of only 51 percent. The Committee understands that NCI is currently supporting research to identify possible risk factors for non-Hodgkin's lymphoma, including a case control study investigating the role of immune suppression and stimulation in non-Hodgkin's lymphoma incidence. The Committee encourages NCI to make the investigation of risk factors for non-Hodgkin's lymphoma a high priority and evaluate the possibility of a workshop to assess the state of knowledge of the causes of the disease.

Multiple Myeloma—Multiple myeloma is unique among all cancers in that the progress of the disease can be tracked from its precursor through active stages through markers of abnormal proteins in the blood and urine. The Committee urges NCI to collaborate with NIAMS and NHLBI and expand knowledge of these markers through all available mechanisms, as appropriate, including greater use of translational research activities. The Committee also urges NCI to work with CDC regarding epidemiological data gathering and interpretation.

Natural Products Drug Development—The Committee encourages NCI to enhance the Natural Products Drug Development program, particularly in the area of complementary and alternative medicine. Recent surveys indicate that a majority of cancer patients will include complementary and alternative therapies in their treatment regime. NCI is encouraged to support high quality research proposals investigating cancer therapies such as iscadore and other botanical substances. Ayurvedic, homeopathic, traditional Chinese approaches, and alternative dietary approaches. The Director of the Institute should be prepared to provide a progress report at the fiscal year 2003 appropriations hearings.

Neurofibromatosis—The Committee encourages NCI to strengthen its neurofibromatosis research portfolio in such areas as further development of animal models, natural history studies, therapeutic experimentation and clinical trials through all available mechanisms, as appropriate. The Committee also urges NCI to continue to coordinate its efforts with other Institutes engaged in NF research.

Ovarian Cancer—Ovarian cancer remains one of the deadliest cancers for women, in part due to the lack of effective early screening methods. The Committee urges NCI to expedite current research in screening methods to detect, diagnose, and identify staging of ovarian cancer. The Committee also encourages NCI to fully fund the four ovarian cancer SPOREs and accelerate research in this area through all available mechanisms, as appropriate, including the establishment of additional ovarian cancer SPOREs.

Primary Immune Deficiency Diseases—A symposium held in March 2000 to investigate the relationship between primary immune deficiency diseases and cancer showed that primary immunodeficiency patients have a 200 times greater risk of developing cancer than someone without primary immunodeficiency. The Committee encourages NCI to develop a comprehensive research portfolio in this area. The Director of the Institute should be prepared to provide a progress report at the fiscal year 2003 appropriations hearing. NCI is also encouraged to expand its role in a national education and awareness campaign through all available mechanisms, as appropriate.

Prostate Cancer—Cancer of the prostate is the most commonly diagnosed non-skin cancer in America and tends to disproportionately affect men who are members of minority groups. If detected early, it can be treated successfully with no negative impact on the cancer survivor's quality of life. However, existing forms of detection are insufficient, and available treatments frequently result in erectile dysfunction, urinary problems, or other disorders and disruptions that negatively impact the patients quality of life. The Committee urges NCI to place an increased priority on research through all available mechanisms, as appropriate, including clinical trials that result in earlier, more reliable detection methods and more effective and less disfiguring treatment regimes.

NIH Office of the Director

The Committee provides $232,098,000 for the Office of the Director, which is $43,752,000 above the fiscal year 2001 comparable level and the same as the budget request. The bill includes language proposed by the Administration and included in the 1998 through 2001 appropriations bill authorizing the collection of third party payments for the cost of clinical services.

Office of Research on Women's Health—The Committee urges the Director to continue to provide fiscal and administrative support that will permit the Office to serve as the central focus for all NIH on women's health research and career development. The additional funding provided in fiscal year 2002 will permit the Office to continue to enhance, stimulate, and co-fund meritorious research on sex and gender factors in basic and clinical studies. These funds should also be used for new research activities in a variety of health issues and new and expanded career development programs for women scientists, such as BIRCWH. The Committee also urges ORWH to enhance research on multi-systemic diseases in women through all available mechanisms, as appropriate, including the establishment of interdisciplinary research centers. The Director should be prepared to provide a progress report at the fiscal year 2003 appropriations hearing.

Office of AIDS Research—The Office of AIDS Research is responsible for coordination of the scientific, budgetary, legislative, and policy elements of the NIH AIDS research program. The OAR develops a comprehensive plan for NIH AIDS-related research activities which is updated annually. The plan is the basis for the President's budget distribution of AIDS-related funds to the Institutes, centers and divisions within NIH. The Committee expects the Director of NIH to use this plan and the budget developed by OAR to guide his decisions on the allocation of AIDS funding among the Institutes. The Director of NIH also should use the full authority of his office to ensure that the ICDs spend their AIDS research dollars in a manner consistent with the plan. The Committee has included the same general provisions in bill language that was contained in the 2001 appropriations bill. This language permits the Director of OAR, jointly with the Director of NIH, to transfer between ICDs up to three percent of the funding determined by NIH to be related to AIDS research.

Office of Behavioral and Social Sciences Research—The Office of Behavioral and Social Sciences Research provides leadership and direction for the development of a trans-NIH plan to increase the scope of and support for behavioral and social science research and in defining an overall strategy for the integration of these disciplines across NIH institutes and centers; develops initiatives to stimulate research in the behavioral and social sciences arena and integrate a biobehavioral perspective across the research areas of NIH; and promotes studies to evaluate the contributions of behavioral, social and lifestyle determinants in the development, course, treatment, and prevention of illness and related public health problems.

The Committee is concerned that, outside of its traditional home at NIMH and a number of other Institutes, there is insufficient NIH support for behavioral and social science investigators. Behavioral science is often treated only as a core mental health, alcohol, or substance abuse field rather than as a core NIH research discipline. Yet, many of the Nation's leading health concerns addressed throughout NIH are behavioral in origin or in their manifestation, including heart disease, lung disease, many forms of cancer, diabetes, developmental disabilities, brain injury, and AIDS. The Committee is pleased that several Institutes such as NCI and NIAMS have begun to expand their behavioral and social science programs. However, NIH should continue to integrate and expand behavioral and social perspectives through its research portfolio. The Committee requests NIH to report back with a plan for a coordinated system of increased training in basic and applied behavioral and social research, a plan for increasing basic and applied behavioral research support in non-traditional institutes, and other measures intended to ensure that NIH scientific priorities and policies appropriately reflect the central role of behavior in health.

The Committee encourages OBSSR to enhance the mind-body initiative to assist the various healthcare fields to understand the existing research on health and spirituality and its clinical implications through all available mechanisms, as appropriate, including the establishment of a coordinating body.

Bayh-Dole Act—The Committee continues to support the principles of the Bayh-Dole Act with respect to the utilization, commercialization and public availability of government funded inventions. As such, the Committee believes that patent protection may be necessary for the development of a research tool as a potential product for sale and distribution to the

research community. However, the Committee is also concerned that products that are a result of Federal funding, especially those discoveries that should be the subject of widespread research, should not be restricted in their use, but should be available to the research community and the public. Therefore, recipients of NIH grants should not be discouraged from seeking patent protection, where appropriate, to bring a product to practical application, but should also license the intellectual property in a manner that maximizes the potential for broad distribution of the research tool. Intellectual property restrictions can stifle the dissemination of new discoveries and limit future avenues of research and product development. At the same time, reasonable restrictions on the dissemination of research tools are sometimes necessary to protect legitimate proprietary interests and to preserve incentives for commercial development. Accordingly, NIH should continue to offer guidance to both funding recipients and their commercial sponsors to find the appropriate balance between these potentially competing interests.

Breast Implants—The Committee is aware of a recent Food and Drug Administration study revealing alarmingly high rupture rates in silicone breast implants and that researchers concluded that the relationship of free silicone to development or progression of disease is unknown. The Committee is also aware of the FDA's recent decision to approve saline breast implants. The Committee encourages NIH to support research to expand the understanding of the health implications of both silicone and saline breast implants through all available mechanisms, as appropriate. Such research should, if determined to be scientifically appropriate, include a multidisciplinary, clinical, case-controlled study of women with breast implants for at least eight years whether it be one prosthesis or multiple, and differentiate between women receiving implants for mastectomy, reconstructive or cosmetic purposes.

Clinical Research Loan Repayment—The Committee is concerned about the declining number of physician-scientists pursuing careers in clinical research. The Committee believes that the Clinical Research Enhancement program authorized by Congress last year is important and that tuition loan repayment should be made available to health professionals who are pursuing structured training experience in clinical research; actively engaged in clinical research career development activities with the guidance of a mentor; or conducting clinical research with independent support from NIH. The Committee has provided funds for the loan repayment program authorized in section 487A of the PHS Act concurrent with the budget request. In order to assess the funding needs for fiscal year 2003, the Committee requests data on the number of applications as of May 1, 2002, as well as the number and size of awards made as of September 1, 2002.

Human Stem Cell Research—The Committee received testimony from NIH institute and center directors, representatives of scientific and medical societies, and members of voluntary health organizations about the potential of both adult and embryonic stem cells for improving the lives of those who suffer with a host of disorders, including diabetes, Alzheimer's, Parkinson's, and cardiovascular disease. The Committee understands that a great deal of basic research is required to determine whether this potential can be realized.

It is the Committee's intent that the NIH move ahead expeditiously to implement the President's policy concerning support of scientifically meritorious research involving both adult and human embryonic stem cells. The Committee commends the NIH for moving quickly to negotiate material transfer agreements with holders of existing embryonic cell lines. The Director is requested to keep the Committee apprised of program initiatives as well as research progress concerning adult and embryonic stem cells.

Minority Health Research—The Committee commends NIH's implementation of various programs focused on developing research infrastructure at minority health professions institutions, including Research Centers at Minority Institutions, Extramural Biomedical Research Facilities and the recently established National Center for Minority Health and Health Disparities. Due to the number of new competitive mechanisms at NIH for these research institutions, the Director is encouraged to work with the Director of NCMHD to establish a program of coordination among these various mechanisms to partner minority health professions schools to address their infrastructure needs.

Pediatric Research—The Committee has previously urged NIH to continue to strengthen and expand its portfolio of pediatric research across all Institutes and establish priorities based on the severity and impact of pediatric diseases and on the potential for scientific breakthroughs. The Committee understands that the Acting Director has asked the NICHD Director to co-chair a committee developing

recommendations to operate the Pediatric Research Initiative authorized as part of the Children's Health Act of 2000. The flexibility afforded to NIH in the implementation of the Initiative will facilitate the development of the most effective means to achieve the program's objectives. Within the total provided to NIH, the Committee believes adequate funds are available to continue implementing this activity. The Committee requests that the Director be prepared to provide a status of this initiative at the fiscal year 2003 appropriations hearing.

Centers for Disease Control and Prevention

The Committee provides $4,077,060,000 for CDC, which is $214,287,000 above the fiscal year 2001 comparable level and $380,449,000 above the budget request. Within the funds provided, the Committee assumes a 4.6 percent pay increase.

Chronic disease prevention and health promotion—The Committee provides $722,495,000 for chronic disease prevention and health promotion, which is $27,213,000 below the fiscal year 2001 comparable level and $147,935,000 above the budget request. This program implements research and programs to prevent the leading causes of death and disability (e.g., heart disease and stroke, cancer, diabetes, and arthritis) which are among the most prevalent, costly, and preventable of all health problems. CDC plays a leadership role in coordinating and catalyzing the efforts of numerous public and private partners, which allows CDC to substantially extend its effectiveness in reaching people at highest risk for chronic disease.

Within the total provided, the following funding levels are for the specific program activities identified: heart disease and stroke, $32,727,000; cancer prevention and control, $67,879,000, of which $38,021,000 is for cancer registries, $10,569,000 is for colorectal cancer, $13,046,000 is for prostate cancer, $1,647,000 is for skin cancer and $4,596,000 is for ovarian cancer; diabetes, $57,728,000; arthritis, $13,251,000; health promotion, $8,630,000; tobacco, $101,071,000; nutrition, physical activity, and obesity, $17,988,000; school health, $58,327,000; safe motherhood/infant health including HIV/AIDS, $49,472,000; oral health, $11,678,000; prevention centers, $22,432,000; epilepsy, $6,527,000; iron overload, $489,000; breast and cervical cancer, $189,296,000; and National Campaign to Change Children's Health Behavior, $85,000,000.

The Committee encourages CDC to continue its collaborative efforts with the National Cancer Institute and the National Institute of Environmental Health Sciences on lymphoma data collection to better understand current trends of lymphoma incidence in the United States. The Committee also encourages CDC to consider developing new efforts to educate patients and health care practitioners about the symptoms associated with lymphoma and the challenges of correct diagnosis.

The Committee encourages CDC to plan and implement public awareness programs for orphan cancers for patients and physicians. Such cancers include esophageal, kidney, liver, multiple myeloma, pancreatic and stomach. Patients diagnosed with these cancers have the lowest life expectancy rates of all diagnosed cancers, yet community oncologists generally lack specific knowledge about these malignancies. Public awareness programs would help physicians better identify orphan cancer symptoms and make more accurate, timely diagnoses.

The Committee encourages CDC to integrate epidemiological data of the National Cancer Registries program, NCI SEER data, NIEHS data and other appropriate Federal sources to create reliable baseline information for all cancer-specific sites and more comprehensive statistical data needed to support research, particularly in the orphan cancers.

The Committee encourages CDC to determine the feasibility of integrating hematological, digestive system and genitourinary cancers screening and awareness programs into existing activities.

The Committee encourages CDC to enhance its chronic fatigue syndrome program to include the study of cancers and linkages with immune-deficiency factors such as multiple myeloma.

The Committee commends the leadership of CDC's National Colorectal Cancer Roundtable in promoting the availability and advisability of screening to both health care providers and the general public. The Committee has provided additional funds to continue to expand partnerships with State health departments, professional and patient organizations, and private industry to combat this disease.

National breast and cervical cancer early detection program funds may be used to reimburse for HPV/DNA tests for women with inconclusive or ASCUS Pap test results.

The Committee is aware of the NCI-convened progress review group on hematological cancers and encourages CDC to work with NCI to determine possible areas of collaboration.

In Brief:

Arthur James, Ohio Founder Of Research Institute, Dead

(Continued from page 1)

and the environment. The L&LS grant is part of the Microsoft donation to eight non-profit organizations nationwide totaling more than $7.6 million. . . . **ARTHUR JAMES,** a former president of the American Cancer Society and founder of the Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, died Oct. 22. Among his awards, he received the Horatio Alger Award in 1987, honoring distinguished Americans. ACS presented James with its Medal of Honor for Clinical Research in 1990. "Because of Dr. James' commitment, many cancer patients from Ohio and beyond have benefited from having access to the latest treatments and the highest quality care available," said **David Schuller**, director of The James Cancer Hospital and Solove Research Institute. . . . **WALTER SCOTT** was appointed to the Fox Chase Cancer Center Department of Surgical Oncology. He was associate professor at Creighton University School of Medicine Center in Omaha with appointments in both the Department of Surgery and the Department Preventive Medicine and Public Health. . . . . **MARCIA GRUBER** was appointed vice president of ambulatory care services at Roswell Park Cancer Institute. She was clinical administrative director of the Gastrointestinal Multi-disciplinary Care Center at M.D. Anderson Cancer Center. Her responsibilities at RPCI are to administer all aspects of ambulatory clinics, including clinic and business operations. . . . **MATT LOSCALZO**, cancer pain expert and co-director of the Cancer Pain Service at the Johns Hopkins Oncology Center, received the City of Hope Cancer Center Sarnat Distinguished Humanitarian Award for his work in palliative care and pain management Oct. 26. He has authored articles on cancer pain management and is principal investigator of studies funded by NCI and Open Society Institute. . . . **HHS APPROVED** 13 states' requests to extend Medicaid benefits to uninsured women who are diagnosed with breast or cervical cancer through a federal screening program. Alaska, Arizona, Arkansas, California, Connecticut, Florida, Kansas, Hawaii, Nebraska, Maine, Michigan, Vermont and Wyoming are the most recent states to take advantage of the federal Breast and Cervical Cancer Prevention and Treatment Act of 2000, which allowed states to expand Medicaid coverage to these women who otherwise would not have health coverage. In the year since the law's enactment, HHS has approved this expanded Medicaid eligibility in 32 states.

THE CANCER LETTER

Vol. 16 No. 9
October 2001

Business & Regulatory Report

Formerly "Cancer Economics"

Product Approvals & Applications:

Novartis Submits Gleevec Data To FDA Seeking Approval For Use In GI Tumors

Novartis has submitted a supplementary New Drug Application to FDA, seeking marketing authorization for Gleevec (imatinib mesylate) for the treatment of unresectable and metastatic malignant gastrointestinal stromal tumors.

GISTs are the most common malignant form of sarcoma arising in the gastrointestinal tract.

Historically, GISTs have been very difficult to treat due to their high levels of resistance to treatment with traditional chemotherapy and radiation therapy. For patients with metastatic or unresectable disease, GISTs

(Continued to page 2)

Clinical Trials:

Genitope Therapy In Phase III Trials For Low-Grade B-Cell Non-Hodgkin's

Genitope Corp. of Redwood City, CA, a private biotechnology company, said its idiotype immunotherapy product is in phase III trials at 22 cancer research sites in U.S. and Canada for low-grade B-cell non-Hodgkin's lymphoma with no prior therapy .

The therapy includes a custom-made protein derived from the tumor cells of each patient using the Genitope patented high throughput gene expression technology. The therapy is being studied for its efficacy in delaying the growth and spread of tumors, the company said.

The tumor-derived protein actively recruits immune cells to attack the tumor and leave normal cells unharmed, the company said.

"Studies using this approach have been very encouraging; the data suggest that idiotype immunotherapies may safely and effectively delay the growth and spread of non- Hodgkin's lymphoma tumors," said Julie Vose, study investigator and professor of medicine, Section of Hematology/ Oncology, University of Nebraska Medical Center.

For the Genitope trial, 360 patients will receive a standard chemotherapy regimen and then be randomized, the company said. 240 patients will receive their custom-made idiotype immunotherapy and 120 patients will receive a non-specific vaccine- like therapy. All patients are expected to complete immunization by the end of 2003.

In clinical trials, side effects include inflammation at the site of the injection and flu-like symptoms, the company said. The side effects are believed to be largely due to the immune stimulation. There are ongoing

(Continued to page 4)

Deals & Collaborations:
Pro-Duct Health, Ductal Lavage Maker, Bought By Cytyc
. . . Page 5

Legal Issues:
TAP Settles Federal Civil Suit For $875M
. . . Page 8

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

Novartis Seeks FDA Approval For Gleevec Use In GIST

(Continued from page 1)

represent an incurable malignancy with a median survival of approximately ten to twelve months. Until now, surgery has been the only treatment option, resulting in palliation of the disease.

Gleevec is approved in the US for the treatment of patients with chronic myeloid leukemia in the blast crisis, accelerated phase or in chronic phase after failure of interferon-alpha therapy.

The effectiveness of Gleevec in CML is based on overall hematologic and cytogenetic response rates. Gleevec is approved for marketing in more than 30 countries, including the US, Switzerland and Australia. Gleevec received a positive recommendation by the European Union's Committee for Proprietary Medicinal Products last July.

The submission for U.S. FDA approval is supported by data from a Phase II, open-label, multinational study conducted in 147 patients with unresectable or metastatic malignant GIST, the company said.

Patients were randomized to receive either 400 mg or 600 mg of Gleevec daily for up to 24 months. The overall response rate is 40 percent based on confirmed partial responses at the time of the data cut-off for the submission. An additional 32 percent of patients in this study achieved a clinically significant reduction in tumor size. Altogether, 12 percent of patients progressed in the study, the company said.

The most common adverse events were nausea, diarrhea, periorbital edema, fatigue, muscle cramps, abdominal pain, dermatitis, vomiting, flatulence, lower limb edema, nasopharyngitis, insomnia, back pain, and pyrexia.

Although almost all patients had adverse events reported at least once during the trial, a small percentage had grade 3 or 4 toxicity. Five patients (3.4 percent) withdrew from the study due to adverse events, the company said.

* * *

Atrix Laboratories Inc. (Nasdaq: ATRX) of Fort Collins, CO, said it has submitted a new drug application to FDA for Leuprogel three-month depot, 22.5 mg leuprolide acetate, for advanced prostate cancer.

Atrix is in late-stage development of three Leuprogel products that release leuprolide acetate over a period of one-, three- and four-months using the Atrix Atrigel Depot drug delivery system, the company said. The goal is to reduce testosterone in the body to inhibit the growth of hormone-responsive advanced prostate cancer. The liquid Leuprogel products are injected subcutaneously with a small gauge needle, forming a solid implant in the body that slowly releases leuprolide as the implant is bioabsorbed, the company said.

Earlier this year, Atrix filed an NDA for its Leuprogel one-month depot product, which is under review at FDA, the company said. The Leuprogel four-month depot product is completing phase III trials.

Atrix said it licensed North American marketing rights to Sanofi-Synthelabo and the European marketing rights to MediGene AG. Australian/New Zealand marketing rights went to Faulding Pharmaceutical.

* * *

Bioenvision Inc. (OTC Bulletin Board: BIOV) of New York said it has received IRB approval for a phase II trial of Modrastane for androgen-independent prostate cancer at the Dana-Farber/Partners Cancer Care Inc., Boston.

Bioenvision has signed an agreement with Dana-Faber/Partners Cancer Care Inc., a joint venture non-profit Corp. established by General Hospital Corp., doing business as Massachusetts General Hospital, Brigham and Women's Hospital Inc., and Dana-Farber Cancer Institute, the company said.

Modrastane has marketing approval in the UK

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

World Wide Web: http://www.cancerletter.com

Business & Regulatory Report

Publisher: Kirsten Boyd Goldberg
Editor: Paul Goldberg
Editorial Assistant: Shelley Whitmore Wolfe

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
E-mail: paul@cancerletter.com

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724

Business & Regulatory Report is a supplement to The Cancer Letter. ISSN 1053-9611.

(marketed as Modrenal) for advanced breast cancer, the company said. In clinical trials the drug gave response rates above 40 percent when used as second or third line treatment in post-menopausal women with hormone sensitive breast cancer.

It is the first commercially available drug in a new class of agents that act as estrogen receptor beta (ER(beta)) agonists, the company said. Modrastane modulates binding of hormone to the second estrogen receptor, ER(beta), and to have an allosteric inhibition of ER(alpha).

ER(beta) was first discovered in the prostate and is highly expressed in that organ, the company said. Experimental studies have indicated that ER(beta) may play an important role in controlling prostate growth, said C B Wood, president and CEO of Bioenvision Inc. An agent, such as Modrastane, that modulates hormone binding to ER(beta) could inhibit growth of prostate cancer.

Extending the use of Modrastane to other hormone sensitive cancers is part of the Bioenvision commercial strategy for its receptor modulation platform technology, the company said. The role of Modrastane and related compounds will be examined in ovarian and uterine cancers.

* * *

Celgene Corp. (Nasdaq: CELG) of Warren, NJ, said Revimid, its immunomodulatory drug, has been granted orphan drug designation by FDA for multiple myeloma.

The IMiDs are small molecule, orally available analogs of thalidomide that are more potent and have a better safety profile, the company said.

The analog has greater immunological activity than thalidomide in in vitro studies, the company said. Data demonstrated IMiDs could inhibit the inflammatory cytokines TNF-alpha and interleukin (IL)-1 beta while stimulating the anti-inflammatory cytokine IL-10. They were also reported to enhance T-cell proliferation and IL-2 production in blood.

Revimid and the IMiD pipeline are covered by a comprehensive intellectual property estate of U.S. and foreign issued patents and pending patent applications including composition-of-matter and use patents, the company said.

Revimid is being evaluated as a multiple myeloma therapy in two phase I/II trials at the Arkansas Cancer Research Center and the Dana-Farber Cancer Institute, the company said. Neither sedation nor constipation, common side effects of thalidomide treatment, was observed, the investigators said. Adverse effects noted were mild to moderate rash and reductions in white blood cell counts.

The drug completed the initial phase of a clinical trial in metastatic melanoma, and based on the results, is being expanded to an additional 60 patients who will be treated at greater than 100 mg/day, the company said.

* * *

Corporate Technology Development Inc. of Miami said FDA granted **Enteron Pharmaceuticals Inc.**, its majority-owned subsidiary, orphan drug designation for orBec to prevent graft-versus-host disease,

GVHD affects the skin, liver, and gastrointestinal tract following bone marrow transplants, the company said.

This is the second orphan drug designation for orBec from FDA, the company said. The drug received a designation to treat intestinal GVHD, which is being studied in a multi-center phase III trial. FDA has also granted orBec Fast-Track status for of intestinal GVHD, the company said.

orBec is an oral dual-release formulation of beclomethasone dipropionate, a site-active corticosteroid drug, the company said. BDP was approved by FDA, and is sold by GlaxoSmithKline, as Beconase, in an inhaled and nasal formulation for asthma, allergic rhinitis, and nasal polyposis. orBec allows larger doses of BDP to be delivered to the afflicted gastrointestinal area without systemic side effects associated with other steroids used to treat GVHD, the company said.

According to the National Bone Marrow Transplant Registry, 12,748 allogeneic bone marrow transplants were performed worldwide during the first half of 2001 on forms of cancer including leukemia, as well as several diseases of the immune and hematopoietic system.

* * *

Fischer Imaging Corp. (Nasdaq: FIMG) of Denver, a manufacturing of digital mammography and medical imaging systems, said FDA has granted final marketing approval for its SenoScan full field digital mammography system.

The system incorporates the Fischer Imaging patented slot scanning detector, which provides 100 percent higher resolution and up to 60 percent less radiation dose as compared to any other FDA approved digital mammography system on the market, the company said.

The system is the only digital mammography

system with a field of view large enough to accommodate almost all sizes of breast without epositioning the patient, the company said. It is designed with an open architecture to accommodate new technological developments such as computer aided detection software, tomosynthesis (3-D imaging), and contrast subtraction mammography.

* * *

Genzyme General (Nasdaq: GENZ) of Cambridge, MA, a division of **Genzyme Corp**., said it would begin marketing Thyrogen (thyrotropin alfa for injection) for well- differentiated thyroid cancer in Europe.

Thyrogen is a recombinant human thyroid stimulating hormone, the company said.

The Committee for Proprietary Medicinal Products of the European Medicines Evaluation Agency agreed on a variation to the manufacturing process for Thyrogen, which was necessary for commercial introduction of the product, the company said.

Thyrogen was approved for marketing in Europe last year and has been available on a named-patient basis since then, the company said. Genzyme plans to launch the product on a country-by-country basis, as pricing and reimbursement approvals are obtained, the company said.

Thyrogen was first approved for marketing in the U.S. 998 as an adjunctive diagnostic tool for serum thyroglobulin (Tg) testing with or without radioiodine imaging, the company said. It was developed for use in patients with well-differentiated thyroid cancer who have had their thyroid gland removed. These patients must take thyroid hormone supplements and undergo periodic testing for recurrent or metastatic cancer.

Until the introduction of Thyrogen, patients were required to stop taking their hormone supplements for two to six weeks prior to testing, the company said. The hormone withdrawal raised the level of thyroid stimulating hormone in bloodstream so that residual or recurrent thyroid cancer or metastases could be detected with either or both serum Tg testing and radioiodine imaging, two commonly used methods of screening for thyroid cancer.

Hormone withdrawal causes fatigue, weight gain, constipation, mental dullness, lethargy, depression, and other adverse reactions, the company said. Thyrogen is an external recombinant source of human TSH that can be used with both of these screening methods, allowing patients to remain on their thyroid hormone supplements.

A meaningful risk of missing a diagnosis or underestimating extent of disease remains with Thyrogen-stimulated Tg testing and radioiodine imaging, the company said. Therefore, thyroid hormone withdrawal Tg testing with scanning remains the standard diagnostic modality.

The most commonly observed adverse events associated with the product (>5 percent) are headache and nausea, the company said.

* * *

IVAX Corp. (AMEX:IVX)(LSE:IVX.L) of Miami, said it received generic approval of its abbreviated new drug application for flutamide capsules, in 125 mg strength, for prostate cancer.

It is the generic equivalent of the Schering Corp. Eulexin capsules, the company said. Ivax said it would sell the product through its subsidiary, Ivax Pharmaceuticals Inc. ales of Eulexin Capsules were approximately $48 million in 2000, the company said.

* * *

Matrix Pharmaceutical Inc. (Nasdaq: MATX) of Fremont, CA, said it would submit an application for the approval of IntraDose (cisplatin/epinephrine) injectable gel to the European Medicines Evaluation Agency through its centralized application process.

The IntraDose application will be based on results from two randomized, placebo-controlled phase III studies of recurrent or refractory head and neck cancer, the company said. Matrix said it would submit the application by the end of the year.

* * *

NeoPharm Inc. (Nasdaq National Market: NEOL) of Lake Forest, IL, said it has submitted orphan drug applications for SS1(dsFv)-PE38 for mesothelioma and ovarian cancer. SS1(dsFv)-PE38 is a monoclonal antibody targeted cytotoxin for tumor cells, the company said.

NeoPharm has licensed the exclusive worldwide development rights for the drug from NCI. Phase I trials for SS1(dsFv)-PE38 are being conducted at Oklahoma University Medical Center and NCI, the company said.

Clinical Trials:

Genitope Therapy In Phase III; Pfizer Buys Lexicon Unit

(Continued from page 1)

phase II studies investigating the use of idiotype immunotherapy for aggressive B-cell malignancies, and preclinical development has begun for T-cell

malignancies, the company said.

* * *

Lexicon Genetics Inc. (Nasdaq: LEXG) of The Woodlands, TX, said it has sold its chemical compounds subsidiary, **Lexicon Pharmaceuticals**, to **Pfizer Inc**. (NYSE: PFE) for non-exclusive use in the Pfizer internal drug discovery programs.

Lexicon Pharmaceuticals is the former Coelacanth Corp., a Princeton, NJ-based company acquired by Lexicon Genetics, which uses proprietary chemistry technologies to discover chemical entities for drug development, the company said.

* * *

MGI Pharma Inc. (Nasdaq:MOGN) of Minneapolis said it is expanding its phase II trial of irofulven for refractory or recurrent advanced epithelial ovarian cancer.

The trial expansion criterion was met with a confirmed objective partial response (greater than 50 percent tumor shrinkage) observed in an ovarian cancer patient with refractory disease, the more difficult-to-treat classification of advanced epithelial ovarian cancer, the company said.

"This is a significant observation at this early point in the study because refractory ovarian cancer patients have already failed first-line standard therapy and are considered to be the toughest group of patients to treat," said William McGuire, trial investigator and director of the Cancer Center at Franklin Square Hospital in Baltimore. "To see an objective partial response is extremely encouraging since this patient had previously failed treatments with carboplatin and paclitaxel, and liposomal doxorubicin."

The completion of patient enrollment is expected in 2002, the company said.

Side effects from irofulven include bone marrow suppression, nausea, vomiting, fatigue, and visual disturbances, the company said.

* * *

NeoTherapeutics Inc. (Nasdaq: NEOT, NEOTW) of Irvine, CA, said its oncology subsidiary, **NeoOncoRx**, would begin two phase II studies of Neotrofin in chemotherapy-induced neuropathy.

Both studies will include 50 patients for six months of treatment at NYU Medical Center, the company said. One study will look at the ability of the drug to protect from chemotherapy-induced neuropathy. The second study will look at efficacy in treating neuropathy resulting from chemotherapy.

"Neuropathy is a dose-limiting toxicity of several anticancer drugs, including some of the most used classes of compounds such as vinca alkaloids, platinum compounds and taxanes, and can be severe and debilitating," said Luigi Lenaz, president of NeoOncoRx. "This toxic effect may limit both the individual doses of the drugs, and the duration of treatment that can be safely given. A drug effective in preventing peripheral neuropathy might allow higher doses or more prolonged treatment to be given, resulting in a possible improved effect of the chemotherapy."

Deals & Collaborations:

Cytyc Buys Pro-Duct Health, Ductal Lavage Device Maker

Cytyc Corp. (Nasdaq:CYTC) of Boxborough, MA, has entered into a definitive merger agreement to acquire **Pro-Duct Health Inc.** a privately-held company that has developed an FDA-approved ductal lavage device designed to enhance the evaluation of risk for breast cancer.

The procedure is for women who are at high risk for breast cancer, and is expected to enable the detection of atypical changes in cells lining the milk ducts, where an estimated 95 percent of all breast cancers originate, the company said.

Under the agreement, Cytyc will pay Pro-Duct Health stockholders a combination of 5.0 million shares of Cytyc common stock and $38.5 million in cash in exchange for all of Pro-Duct's outstanding capital stock and vested options and warrants. The 5.0 million shares excludes approximately 150,000 shares that are reserved for issuance upon exercise of outstanding unvested Pro-Duct options being assumed by Cytyc in this acquisition.

The total equity value of the transaction is approximately $167.5 million, the company said.

"We finally have access to where breast cancer starts," said Susan Love, one of the founders of Pro-Duct Health, adjunct professor of surgery at UCLA, medical director of the Susan Love, M.D., Breast Cancer Foundation.

"Women with a statistical increased risk of breast cancer because of family history or genetic mutations can find out whether they have cellular changes at a point when they can explore preventive options," Love said. "The procedure is relatively painless and can be easily repeated periodically in premenopausal and postmenopausal high-risk women giving us the kind of information about changes in the breast that the Pap test has given us about the cervix."

Cytyc manufactures the ThinPrep Pap Test.

"We estimate that the Pro-Duct opportunity represents an initial, annual U.S. market potential of $1.5 billion, growing to $4 billion, and is an ideal fit for Cytyc," said Patrick Sullivan, Cytyc president and CEO. "We have in place the resources and talent in the key areas of sales, marketing, manufacturing, regulatory and clinical affairs, consumer education, and reimbursement that will support further adoption of this important medical advance."

The proprietary ductal lavage catheter developed by Pro-Duct Health has been approved by FDA to be used to collect cells from the lining of the milk ducts. The cell specimen is sent to a laboratory for slide preparation using the ThinPrep System and is then examined by a cytopathologist. The medical rationale for ductal lavage is compelling since a number of investigators, including the inventor of the Pap smear, Dr. George Papanicolaou, have published studies demonstrating that high-risk women with atypical milk duct cells have a significantly increased, near-term risk of developing breast cancer, the company said.

A large-scale, multi-site clinical trial by Dooley and colleagues evaluated ductal lavage using the Pro-Duct catheter, the company said. The study enrolled more than 500 women at high-risk for breast cancer who had nonsuspicious findings on mammograms and physical examinations within the previous 12 months. Atypical cells were detected in 23 percent of the study population. The authors concluded, "Ductal lavage is a safe, well-tolerated, and relatively noninvasive procedure for collecting breast ductal epithelial cells to allow for the determination and differentiation of normal, premalignant, and malignant cytology."

* * *

AxCell Biosciences, a subsidiary of **Cytogen Corp.** (Nasdaq: CYTO) of Princeton said they are about to enter into a CRADA with NCI to research two signal transduction families and their impact on signaling pathways within cancer cells and other diseases.

Under the terms of the pending agreement, data would be added to the AxCell ProChart database of protein interaction information, the company said.

"Faulty signaling in cells is believed to be responsible for many diseases including cancer, diabetes and immune disorders," said John Rodwell, president and chief technical officer of AxCell Biosciences. "A better understanding of the signaling pathways involved with tyrosine and serine-threonine kinases could play a role in developing new and more effective therapies for many disorders."

Stephen Shaw, chief of the Human Immunology Section at the Experimental Immunology Branch of NCI will lead the research, the company said. The research would predict and validate sites of phosphorylation of human proteins, the effects of that phosphorylation on binding interactions of such proteins, and to identify recruitment sites which facilitate peptide phosphorylation by binding to kinase domains at regions distinct from the catalytic cleft, the company said.

The AxCell ProChart database, human cell signaling maps of protein interactions, is marketed exclusively by InforMax Inc., the company said. By year-end, the database could contain protein pathway information from several other domain families, such as PDZ, SH2 and SH3 domains.

ProChart is available to pharmaceutical and biotechnology company subscribers on a corporate-wide basis, across all therapeutic programs and several phases of drug discovery and development from target identification and validation to lead compound prioritization, the company said.

* * *

Bristol-Myers Squibb Co. (NYSE: BMY) said it has acquired **DuPont Pharmaceuticals Co.** from **DuPont** (NYSE: DD) for $7.8 billion in cash.

With the acquisition, BMS gains in-line products, including Sustiva, the non-nucleoside reverse transcriptase inhibitor for HIV/AIDS; Coumadin, an oral blood anticoagulant; and Cardiolite, a leading cardiovascular medical imaging agent, the company said. BMS also gains an R&D pipeline that includes compounds in five therapeutic areas—virology, cardiovascular diseases, inflammatory diseases, cancer and disorders of the central nervous system.

The transaction is expected to be accretive to earnings per share beginning in 2003, the company said. In 2002, it will be dilutive to EPS by between zero and three cents. In 2003, the transaction will be accretive to EPS by between six and eight cents. In years following 2003, the annual EPS growth rate will be significantly enhanced, probably in the range of two percentage points per year.

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

In addition to the DuPont Pharma acquisition, the company already has announced the sale of its Clairol haircare business, spun off its Zimmer orthopaedic implants business and agreed to invest in

ImClone Systems and to co-develop and co-promote IMC-C225, the ImClone investigational cancer therapy.

* * *

Endocare Inc. (Nasdaq: ENDO) of Irvine, CA, said it has entered into a new expanded distribution agreement with **Qualigen Inc**, a privately held company of Carlsbad, CA, to expand the existing OEM agreement for the Qualigen physician office lab system.

Under the agreement, Endocare will sell the Qualigen FDA-cleared, 15-minute total prostate specific antigen test as a stand-alone product, non-exclusively directly to urology practices, the company said.

The test provides rapid, fully-automated, laboratory quality PSA test results in physician office laboratories. An estimated 25 million PSA tests are performed in the U.S. annually, the company said.

Endocare said the Qualigen FDA-cleared fastpack system provides a step forward in prostate diagnostics, eliminating the several day wait in determining a PSA test result, the company said.

Endocare said it plans to use the fastpack system in newly developed regional prostate cancer centers, which will be called TCAP Regional Centers of Excellence. The centers, slated to operate at prominent medical centers across the nation, are for men who have undergone radiation therapy for prostate cancer and whose cancer has returned.

* * *

GE Medical Systems of Waukesha, WI, and **US Oncology** of Houston said they have signed a multi-year partnership agreement in which US Oncology will buy the GE Advance NXi positron emission tomography systems for service sites in 27 states.

The GE Advance NXi system is capable of imaging with all PET tracers, as well as provide image quality, high throughput, easy operator interaction and reliability with its built-in remote diagnostics, the company said.

* * *

Genmab A/S (CSE: GEN and Neuer Markt: GE9D) of Copenhagen said it has entered a collaborative agreement with **Immunex Corp.** (Nasdaq: IMNX) to discover and develop a fully human antibody against a proprietary Immunex cancer target for lymphoma.

HuMax-Lymphoma will target the IL-15 receptor, which is found on a number of tumor types, including T cell and natural killer cell lymphomas, as well as multiple myeloma, the company said. The cytokine IL-15 contributes to cell growth and proliferation and helps prevent programmed cell death. Blocking tumor receptors for IL-15 with HuMax-Lymphoma could result in specifically targeted anti-cancer therapy.

Under the agreement, Genmab will be responsible for the antibody, to be called HuMax-Lymphoma, through phase II trials, the company said. Immunex retains an exclusive option for the product through phase II. Should Immunex exercise its option, the company would complete the clinical development of the antibody and would pay a license fee, milestones and share profits upon commercialization. Alternately, Genmab will retain the right to continue to develop and potentially commercialize the antibody and would pay milestone fees and royalties to Immunex, the company said.

* * *

Hybrigen Inc. of Dallas and **Bionomics Ltd.** (ASX: BNO) of Adelaide, Australia, said they have signed a letter of intent to collaborate on breast cancer discover drug targets.

The program focus is on two genes, TSG18 and BNO1, identified and patented by Bionomics, the company said. TGS18 is undergoing study as a breast cancer tumor suppressor gene; BNO1 induces programmed cell death in breast cancer cells.

Hybrigen said it will use its proprietary proteomic technologies for drug targets that interact with the genes. The companies said they will co-own the drug targets developed in the program.

* * *

Immusol of San Diego said it has signed a five-year, oncology discovery and development collaboration with **Novartis Pharma AG** (NYSE: NVS).

The collaboration could be worth $150 million to Immusol depending on the targets delivered and successful compound development by Novartis. Also, as part of the agreement, Novartis becomes an equity investor in Immusol, the company said.

Immusol will identify pharmaceutically relevant drug targets from biological assays in defined cellular and in vivo systems and Novartis will use these biologically verified targets to develop compounds for major unmet oncology indications, the company said.

The collaboration would identify drug targets associated with tumor suppression, repressors of tumor suppression, inhibition of apoptosis, and other oncogene pathways, the company said.

* * *

PDI Inc. (Nasdaq: PDII) of Upper Saddle River, NJ, said it has signed an agreement with **Eli Lilly and Co**. (NYSE: LLY) to co-promote Evista (raloxifene HCl) in the U.S. for several applications including the reduction of invasive breast cancer.

Under the agreement, PDI will provide sales representatives to co-promote Evista to U.S. physicians, the company said.

* * *

Raven Biotechnologies Inc. of South San Francisco said it has delivered the first in a series of candidate monoclonal antibodies for evaluation by **ImmunoGen Inc.** (Nasdaq: IMGN) of Cambridge, MA.

Legal Issues:

TAP To Pay $875 Million To Settle Federal Civil Suit

TAP Pharmaceutical Products Inc. of Abbott Park, IL, has agreed to pay $875 million to settle criminal charges and civil liabilities in connection with its fraudulent drug pricing and marketing conduct with regard to Lupron, federal prosecutors said.

The company agreed to plead guilty to a conspiracy to violate the Prescription Drug Marketing Act and settle its federal civil False Claims Act liabilities for filing false and fraudulent claims with the Medicare and Medicaid programs as a result of TAP's fraudulent drug pricing schemes and sales and marketing misconduct. The company also committed to a corporate retraining program, the agreement states.

At the same time, a federal grand jury returned an indictment unsealed today, charging one physician and six TAP managers with conspiracy to pay kickbacks to doctors by causing free samples to be illegally billed to the Medicare program.

The indictment charges that the TAP defendants offered to give things of value, including free drugs, educational grants, trips to resorts, free consulting services, medical equipment, and forgiveness of debt, to physicians and other customers to obtain their referrals of prescriptions for Lupron to Medicare program beneficiaries, in violation of the anti-kickback statute.

Prior to the indictment, four other physicians have been charged and have pleaded guilty in the investigation, officials said. The investigation commenced in the District of Massachusetts in 1997 after a urologist employed by Tufts Associated Health Maintenance Organization in Waltham, Joseph Gerstein, reported to law enforcement authorities that he had been offered an educational grant if he would reverse a decision he had made on behalf of Tufts that it would only cover the less expensive drug Zoladex, officials said.

The investigation was also triggered by a civil False Claims Act suit filed in 1996 by Douglas Durand, after he had quit his employment at TAP as vice president of dales.

Gerstein, Durnad, and Tufts Associated HMO will share as whistleblowers the rective in the False Claims Act, 17% of the civil recovery, or an amount of approximately $95 million.

Thomas Watkins, president of TAP Pharmaceuticals, said the company disagrees with many of the government's allegations. "We fundamentally we resolved this matter to make clear our commitment to proper and ethical business practices, and to avoid protracted legal battles and ensure uninterrupted availability of Lupron for many thousands of patients who rely on it."

Watkins acknowledged that in the early to mid-1990s TAP provided samples of Lupron physicians with the knowledge that those physicians would seek reimbursement. "The billing for free samples is wrong, and it should never have happened," he said. "We have taken strong action so that this inappropriate marketing practice will never happen again."

* * *

IMPATH Inc. (Nasdaq: IMPH) of New York said it has agreed to preliminary terms with the U. S. Department of Justice with regard to its investigation involving claims submitted by the company to federally financed health care reimbursement programs from 1990 through 1998 for one of the tests necessary to perform Impath's diagnostic and prognostic services.

The company said it has agreed to pay the government $9 million without any admission of wrongdoing and will receive a release of claims upon the execution of definitive documents.

"We firmly believe that our billing and laboratory practices meet all applicable regulations and we continue to maintain a rigorous program to ensure ongoing compliance," said Anu Saad, chairman and CEO. "However, a lengthy proceeding would continue to drain valuable corporate resources and would unduly distract management from the company's primary mission of providing information to physicians and the pharmacogenomic industry to improve the lives of patients with cancer."

February 13 -17, 2002

Chateau Whistler

Whistler, British Columbia, Canada

Sixth Annual *Winter Oncology Conference*

Advances in Hematological Malignancies and Supportive Care in Cancer

Program Directors

Vinay Jain, MD, FACP
Baylor-Charles A. Sammons Cancer Center
Dallas,TX

Marvin Stone, MD, MACP
Baylor-Charles A. Sammons Cancer Center
Dallas, TX

Martin Tallman, MD
Northwestern University Medical School
Chicago, IL

Welcome to the Sixth Annual Winter Oncology Conference to be held at the Chateau Whistler in Whistler, British Columbia from February 13-17, 2002. This 4½ day conference will focus on hematological malignancies in oncology and supportive care in cancer. A distinguished faculty will present cutting edge data on recent advances in the diagnosis and management of hematological malignancies, including acute and chronic leukemias, lymphomas (Hodgkin's and non-Hodgkin's), myeloma, and also thrombotic disorders. The conference will also focus on supportive care in cancer issues, including management of chemotherapy-induced toxicities, newer antibiotic and antifungal drugs, use of newer cytokines for immune enhancements, improvement in quality of life, pain control, and other important topics. The goal of the meeting will be to update attendees of developments that have taken place over the last 12 months, since our last hematological malignancies and supportive care in cancer conference.

Who should attend?

This educational program is intended for medical oncologists, hematologists, and other physicians with an interest in recent advances in hematological malignancies and supportive care in cancer. No specific skills or knowledge other than a basic training in medicine is required for successful participation in this activity. Fellows, nurses, and pharmacists in the oncology field are also invited to attend.

Registration Form

SIXTH ANNUAL WINTER ONCOLOGY CONFERENCE

Return by fax to 214-818-7463

For more information call 214-818-7462 or visit www.cancerconferences.com

First Name _____ Last Name _____ Credentials _____

Mailing Address _____ Suite _____

City _____ State _____ Zip Code _____

Last four digits of SS Number _____ Phone ( ) _____ Fax ( ) _____

Please check the appropriate category	*Before Nov. 30, 2001*	*Dec. 1 – Jan. 8, 2002*	*After Jan. 8, 2002*
❑ Physicians	❑ $295.00	❑ $395.00	❑ $495.00
❑ Fellows, Nurses, Pharmacists, Others	❑ $195.00	❑ $195.00	❑ $195.00

❑ Check here if you have any special dietary needs.

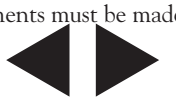
Please specify:_____

Payment may be made by: [ ] Check [ ] Visa [ ] MasterCard [ ] Discover [ ] American Express

Card Number _____ Expiration Date _____

Name as it appears on charge card_____ Signature_____

Please make checks payable to PHYSICIANS' EDUCATION RESOURCE. All payments must be made by a draft on a United States Bank.



Copying Policy for The Cancer Letter Interactive

The software that comes with your issue allows you to make a printout, intended for your own personal use. Because we cannot control what you do with the printout, we would like to remind you that routine cover-to-cover photocopying of The Cancer Letter Interactive is theft of intellectual property and is a crime under U.S. and international law.

Here are guidelines we advise our subscribers to follow regarding photocopying or distribution of the copyrighted material in The Cancer Letter Inc. publications in compliance with the U.S. Copyright Act:

What you can do:

--Route the printout of the newsletter to anyone in your office.

--Copy, on an occasional basis, a single story or article and send it to colleagues.

--Consider purchasing multiple subscriptions. Contact us for information on multiple subscription discounts.

What you can't do without prior permission:

--Make copies of an entire issue of the newsletter. The law forbids cover-to-cover photocopying.

--Routinely copy and distribute portions of the newsletter.

--Republish or repackage the contents of the newsletter.

We can provide reprints for nominal fees. If you have any questions or comments regarding photocopying, please contact Publisher Kirsten Boyd Goldberg, phone: 202-362-1809, email: kirsten@cancerletter.com

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

Click Here for
Photocopying Guidelines