THE CANCER LETTER INTERACTIVE

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House And Senate Appropriators Pledge To Increase Biomedical Research Funding

Members of the House and Senate subcommittees that appropriate funds for NIH pledged at hearings last week to find additional money for biomedical research, to supplement the 2.1 percent increase proposed by the Clinton Administration.

In addition to promising more money for NIH, members of both committees seemed eager to find creative ways to prompt NIH Director Harold Varmus and NCI Director Richard Klausner to make the point that additional money would buy more (and better) science.

The multibillion-dollar question in this game of softball on Capitol

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In Brief:

Schilsky Promoted To Associate Dean At Chicago, Vogelzang To Direct Center

RICHARD SCHILSKY plans to step down as director of the University of Chicago Cancer Research Center to become the university's associate dean for clinical research, a newly created position, effective July 1. Schilsky directed the cancer center for the past eight years. He will continue as chairman of the Cancer and Leukemia Group B. Schilsky also will become chairman of the FDA Oncologic Drugs Advisory Committee, effective July 1, for the final year of his term on the committee. He replaces **Janice Dutcher**, of Our Lady of Mercy cancer center, Bronx, NY, who completed her term. **NICHOLAS VOGELZANG** will succeed Schilsky as the cancer center director. Vogelzang is associate director for clinical research at the center and chairman of the CALGB Prostate Cancer Committee.. . . **MARY J.C. HENDRIX** was elected president-elect of the Federation of American Societies for Experimental Biology. Hendrix is professor and head of the Department of Anatomy and Cell Biology, University of Iowa College of Medicine, and associate director of basic science research at University of Iowa Cancer Center. She will become president of the Federation on July 1, 2000. Hendrix represents the American Association of Anatomists on the FASEB Board. She is also a member of two other FASEB societies, the American Society for Investigative Pathology and the American Society for Cell Biology. She is also a member of the American Association for Cancer Research. . . . **BERT VOGELSTEIN**, Clayton Professor of Oncology at Johns Hopkins Oncology Center and investigator for the Howard Hughes Medical Institute, received the 1998 Louisa Gross Horwitz Prize from Columbia

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Appropriators Ask NIH, NCI: Could You Use More Money?

(Continued from page 1)

Hill is whether pledges of support from both sides of the aisle would translate into a bigger increase for NIH. Some clues about the answer are likely to materialize within a few weeks, in the course of debates over the budget resolution.

Always an important part of the process, the resolution is especially important this year, since Republicans are becoming amenable to raising the budget caps that limit government spending, sources said. With surpluses projected for the near future, legislators are considering a tax cut, increases in spending on defense and education, as well as revamping the financing of Social Security and Medicare.

Remarks by legislators at the NIH hearings appear to indicate that by comparison with these big-ticket items, a few extra billion for NIH doesn't seem like much—at least at this stage. At the very least, discussion of the NIH budget gives legislators an opportunity to snipe at the Administration for its paltry proposal for biomedical research.

"Congress has consistently taken a more generous look at NIH funding than has the Administration," Sen. Arlen Specter (R-PA), chairman of the Senate Labor, HHS & Education Appropriations Subcommittee said at a hearing Feb. 23. "This year is going to be tougher than ever to find funding that is going to keep the kinds of applications rolling. I do know that if the funds are not very substantial, it will cut back on the kind of research projects you have.

"We are going to do our utmost, but I would urge everyone in this room to communicate with the chairman of the budget committees of both houses, and the appropriations chairmen, to have the allocations that is what it takes for this subcommittee to make the baseline recommendations," said Specter, a cancer survivor.

Sen. Tom Harkin (D-IA), the ranking minority member of the subcommittee, agreed.

"I am sure that we all agree, at least up here, that the NIH budget is woefully inadequate," Harkin said at the same hearing. "The 2.1 percent increase has got to be raised, and hopefully, we are going to find some way to do it. I don't know how, but that needs to be addressed. I am a little dismayed that we can't find the money to meet the research and health needs of our people, but we can find more money for re-invigorating the Star Wars program."

Sen. Ted Stevens (R-AK), chairman of the full appropriations committee, urged HHS Secretary Donna Shalala to find a way to increase NIH funding. Stevens said he was particularly interested in scaling up the NCI prostate cancer program. "[The Administration's proposal] is not even the rate of inflation," Stephens, a prostate cancer survivor, said at the hearing. "I want to make sure that the [prostate cancer] initiative doesn't stall out."

Summing up at the House subcommittee hearing Feb. 24, Rep. John Porter (R-IL), chairman of the Labor, HHS and Education Appropriations Subcommittee, pledged to do better than the Administration. "Dr. Klausner, you are doing a magnificent job at NCI," Porter said. "We do want to give you the resources that you need and your investigators need to help cure this disease or find a way to prevent it."

Administration: NIH Got Its Raise In Advance

In testimony before the appropriations subcommittees, Varmus and HHS Secretary Donna Shalala said the budgets for the fiscal years 1999 and 2000 should be considered as a "package." Last year, NIH got a 15 percent increase, nearly double the increment required to reach the Administration goal to increase the NIH budget by 50 percent from 1998 to 2003.

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"We are viewing 1999 and 2000 as a kind of package, in which the money that the President slated for the year 2000 was achieved in 1999, and the differences among institutes were reflected in the differences that were found in the 1999 budget," Varmus said at the House hearing.

Varmus said the budget proposal would allow NIH to continue the work begun in 1999.

Under the President's budget, NIH would finance about 7,600 new and competing R01 grants in the year 2000, Varmus said. That would represent a decline from the current year's level of just under 9,200, he said.

The drop would bring the number of grants to the 1998 level, Varmus said. "But remember, 1998 [was] a reasonably good year," he said. To maximize the funds available for grants, NIH has instituted a fiscal management strategy that involves not increasing the sizes of grants and foregoing an inflationary adjustment, Varmus said.

"We have generated enough money to be able to pay a substantial number of new grants in the year 2000," Varmus said. "What we obviously can't do is increase the number of new awards, and in certain new programs where we would ordinarily consider starting 50 awards in a new area in one year, and have another 50 new awards in the following year, that will be more difficult to do."

Asked by Specter to reveal his "professional judgment" budget, Varmus said NIH could use as much as $19.3 billion, $3.4 billion more than the President's request of $15.9 billion.

"We like your professional judgment, Dr. Varmus," said Specter. "We understand the constraints of the Office of Management and Budget. And we understand you are a team player. But the $19.3 figure is what you think you need in order to carry out the research and handle the applications and grant requests."

VARMUS: "That number represents what we can do under optimal fiscal conditions, if we were to exploit, in a reasonable way, all of the opportunities that are before us. We do think we can operate effectively under the President's budget, and under many intermediate phases of funding."

SPECTER: "We understand you are a team player, but we appreciate the other figure, so we have a guidepost. I think what I asked you privately that we can out in the record here, the $2 billion that has been added [in FY99] is a figure that you can assimilate, and can use efficiently. Correct?"

VARMUS: "Absolutely. We have documented that very carefully in 1999. The tables are provided to you."

Prior to the hearings, Capitol Hill observers said NIH would be challenged on its ability to make use of the current year's $2 billion increase. However, this challenge did not materialize at the Senate and the House hearings.

The hearings were timed fortuitously for NCI. A day earlier, the New England Journal of Medicine announced the findings that chemotherapy and radiation can cut cervical cancer mortality by about 30 to 50 percent, and the Institute issued a clinical alert about the findings.

"Let me ask for a very brief response from Dr. Klausner on the headlines today about cervical cancer mortality could be cut by half with chemotherapy and radiation," said Specter. "What is the prospect of further advances like this if you get your optimal budget, contrasted with the OMB budget?"

KLAUSNER: "The announcement that was made yesterday was the result of five NIH-funded clinical trials. It's an example of the productivity of the clinical trials system."

SPECTER: "It was not timed for this hearing?"

KLAUSNER: "It was not. It should have been. Coincidences… There is no question that our clinical trials system, our drug development, drug discovery system will allow us to make these sorts of advances."

SPECTER: "I compliment you, Dr. Klausner, on that. That's why we want to back you up."

Porter: IOM Coding Proposal "Illogical"

Addressing one of the few truly controversial issues raised at the hearing, Varmus and Klausner vehemently disagreed with the coding recommendations contained in the recent Institute of Medicine report on cancer in minorities and the underserved.

After both Varmus and Klausner said the numbers cited in the report were inaccurate and the recommendation that NIH change its coding of grants unacceptable, Porter agreed, saying that the report's recommendation that only projects that address research questions related to minorities should be coded as minorities research sounded "illogical."

"I think I agree with you on that," said Porter to Klausner. "Obviously, I don't know enough about it, but it sounds illogical and doesn't make any sense. The way you are doing it sounds like it does."

Porter's comments followed Klausner's

strongly worded challenge of accuracy of the report and usefulness of its recommendations.

Klausner said he is still puzzled by the statement in the report that NCI spends $24 million on research in minorities.

"We don't understand what got lost in the transfer [of information] from NCI to IOM," Klausner said. "There are 189 projects that we code as 100 percent directed at answering questions related to the unequal burden of cancer in minorities and the underserved. That comes to $64 million. We don't know where their $24 million number came from.

Klausner disagreed with the report's most controversial recommendation that only research exclusively targeted at minorities should be coded as minorities research by the Institute.

"We are not trying to over-claim how much we are spending," Klausner said. "Let me give you some examples of projects the IOM refused to count because they were only partially funded. A project called Racial Differences in Breast Cancer Survival that compares Caucasian women with others, and we code that as 28 percent minority. Black/White study of prostate, multiple myeloma, pancreatic, esophageal cancers. We coded that 50 percent.

"Another thing essential to any approach to understanding the unequal burden of cancer is our surveillance system," Klausner said. "The SEER system that over-samples minorities so we can get good information. Part of SEER are dollars spent answering the most basic questions address by the IOM report. But they say none of the dollars that support SEER should be counted as giving us the information that that report tells us we have to get, because the SEER program isn't one surveillance program only for the minorities, and another for non-minorities.

"We think that makes no sense. Partial coding, which we always do, is not dishonest. It's not a gimmick. We feel very comfortable about the correctness of what we are spending," Klausner said.

"I think it would be a big mistake to move to the coding system as used in the IOM report," Klausner said.

Sullivan's Proposal On Minorities Research

At the House hearing, Rep. Jesse Jackson (D-IL), read a portion of a letter from former HHS Secretary Louis Sullivan.

The Sullivan proposal, described in a Feb. 19 memo to Specter, calls for enhancing the authority of the NIH Office of Research on Minority Health and the NCI Office of Special Populations Research. Moving beyond the scope of the IOM recommendations, Sullivan writes:

—"The NIH Office of Research on Minority Health should be elevated to [NIH] center status, much the same way that the Office of Alternative Medicine was recently elevated to the National Center for Complementary and Alternative Medicine. The new National Center for Research on Minority Health should be given the authority and the resources to assume a leadership role across NIH in developing a strategic plan for research into those diseases and disorders which disproportionately affect the nation's minority populations. It should also have the authority to make grants from its own budget for important research affecting minority health without having to go through the existing institutes. It should retain the right to collaborate with the institutes, but should no longer be subservient to their judgment about minority health initiatives.

—"The NCI Office of Special Populations [Research] should be given the authority to make grants, convene scientific peer review panels, set priorities for the other divisions, and hold them accountable for supporting minority health research programs. The office has to be given a distinct and discretionary budget (not a line item) within the NCI's annually appropriated budget. In addition, the OSP director should be made a member of the NCI Executive Committee, to assist the NCI Director and other NCI colleagues in developing the NCI research agenda."

Sullivan, president of the Morehouse School of Medicine and the principal investigator of the NCI Black Leadership Initiative, said the two offices, which have not seen funding increases in several years, should be given the same proportional increases as NIH and NCI.

Responding to a question from Jackson at the House hearing, Varmus said he opposed elevating ORMH to center status.

"The ORMH has been an effective instrument to coordinate research among the institutes, and to look for deficiencies in their programs," Varmus said. "As you know, if one analyzes the NIH budget with respect to spending on minority health, the number is well over $1 billion.

"My view is that that activity, while extremely important and in need of continual surveillance, is an activity that is best undertaken by every institute,"

Varmus said. "I would be concerned about trying to segregate those activities into a separate center. My initial inclination is to believe that we need to inspire every institute to be heavily involved in understanding the impact of all of our diseases on all of our minority populations."

Jackson disagreed.

"My goal would not be to segregate health research," he said. "The goal would not be to create a strategic plan across [NIH]. Furthermore, that also gives that entity grant-writing powers. For example, sickle cell anemia is a disease that might be found only in a population. A Historically Black College may have an interest in a minority population, and a minority group of doctors who might specifically be focusing their research on trying to resolve a disease that has an implication for only that minority population. I am not suggesting that anything at NIH should be segregated, but certainly, better coordination and planning at the center level might be something that we should look into in the future."

Later at the hearing, Jackson said he was fascinated to see this proposal come from Sullivan.

"What I find so fascinating is that the former head of HHS is now the president of the Morehouse School of Medicine, and from his perspective of being in the field, he is confronting something that he probably could have resolved when he was the Secretary of HHS," Jackson said.

According to an optimistic schedule advanced by the House and Senate leadership, the debate over the budget resolution is expected to conclude sometime before April 15, sources said. By June 1, the 13 appropriations subcommittees would try to complete their work. The Senate target for completion of markup is the end of July, sources said.

Clinical Trials:

NIH, Health Plans Association, Agree In Principle To Raise Clinical Trial Enrollment

NIH and the American Association of Health Plans said they have taken a first step toward the development of specific agreements by health plans to pay the patient care costs for members participating in clinical trials.

Under the terms of the agreement by NIH Director Harold Varmus and Karen Ignani, president of AAHP, the AAHP and its member plans will work with NIH to develop a process that will increase participation in NIH-sponsored clinical trials. An important part of the implementation of this agreement will be NCI's efforts to ensure access to cancer clinical trials.

The agreement is based on a set of jointly held principles stating that clinical trials are the most effective means of generating reliable evidence relating to medical interventions; NIH is committed to supporting the conduct of this research as the means of identifying therapeutic advances that are then translated into standards of patient care; health plans have the potential to create new opportunities to increase patient accrual, conduct clinical research, disseminate research findings, and incorporate research advances into routine medical practice; AAHP is committed to increasing the participation of plan members in well-designed, high quality clinical trials; and plans are more likely to facilitate and encourage clinical trials participation if it is not markedly more expensive to the plan than standard clinical care.

In a report to Congress last year, NCI Director Richard Klausner said the reluctance of health plans to help pay for the care of people in clinical trials had become "a serious barrier to progress" in cancer research. "It is the legitimate responsibility of the insurance industry to reimburse the costs of routine medical care of cancer patients in all phases of high-quality research trials," Klausner said.

The agreement is a statement of intent and its success will depend on the commitment of the health plans to developing specific coverage arrangements with clinical research groups, NIH and AAHP said.

A steering committee consisting of five representatives of the NIH, five representatives of AAHP, and three patient advocates will oversee the research activities and will evaluate progress made under the agreement on a yearly basis.

Cancer Screening:

Americans Over 50 Urged To Get Colon Cancer Tests

Three federal agencies this week announced the start of a national campaign to educate Americans 50 and older about the importance of colorectal cancer screening tests for early detection and prevention of the disease.

The Centers for Disease Control and Prevention, Health Care Financing Administration, and NCI

began the Screen for Life campaign as new evidence was published in the Journal of the National Cancer Institute showing significant reduction in colorectal cancer deaths associated with regular screening.

"The good news is that we can prevent many deaths from colorectal cancer through screening," Surgeon General David Satcher said in a March 2 statement. "If you've celebrated your 50th birthday and have never been screened for colorectal cancer, start now to screen for life."

CDC recently released data showing that only 41 percent of men and women age 50 and older are having either of the two most commonly recommended screening tests, home-administered blood stool tests or sigmoidoscopy/proctoscopy, within the recommended time intervals.

As proposed by President Clinton, new Medicare preventive benefits including colorectal cancer screening were enacted in 1997 and went into effect last year. The awareness campaign is aimed at encouraging Medicare beneficiaries and others to take advantage of screening.

"Medicare took a big step forward in covering preventive benefits," said Nancy-Ann DeParle, HCFA administrator. "Now, through Screen for Life, we're able to promote healthy aging and help beneficiaries take an active role in their health."

The Screen for Life campaign includes public service announcements and information materials targeting Americans 50 and older. The campaign also will promote the new Medicare coverage of colorectal cancer screening procedures.

In the March 2 issue of JNCI, researchers at the University of Minnesota reported on an 18-year study which extends their findings that screening for blood in the stool can reduce mortality from colorectal cancer. The team, led by Jack Mandel, professor of public health, found that annual screening with a fecal occult blood test can lead to a 33 percent reduction in mortality, and that screening every two years results in a 21 percent drop in mortality.

CDC and other health organizations, including the American Cancer Society and gastroenterologic organizations, support the blood stool test or a combination of several tests for colorectal cancer screening.

The Screen for Life web site: http://www.cdc.gov/cancer/screenforlife/ To order Screen for Life campaign materials, call 888-842-6355. For more information about Medicare benefits, visit http://www.medicare.gov

Cancer Prevention:

HHS Calls For Warning Labels On Cigars, Says Teen Use High

The U.S. Department of Health and Human Services issued a pair of reports last week by the HHS Inspector General warning about cigar use among teenagers and recommending mandatory warning labels similar to those on cigarettes and other tobacco products.

"These reports add to our department's growing understanding of the dangers of cigar smoking," said HHS Secretary Donna Shalala. "The new information in these studies will help us with our ongoing efforts to reduce teenage smoking and youth access to tobacco products of all kinds, and I am pleased that the Surgeon General has agreed to review the issues these reports raise."

The Office of the Inspector General study on "Patterns of Use and Perception of Risk" included 18 focus groups involving a mix of 227 young cigar users and non-users of different socioeconomic backgrounds from urban and suburban areas across the country. Thirteen of the focus groups comprised high school students, four involved junior high students, and one was made up of college students. The purpose of the focus groups was to explore patterns of cigar use among the participants and their peers. Specific questions focused on initiation, frequency, and variations of use, as well as the motivations and influences to use cigars.

The study found that more than a third of the teenagers who participated in the focus groups admitted to having smoked a cigar in the past 30 days, and half of the smokers said they expect to be cigar users five years into the future. They further reported widespread cigar use and experimentation among their peers and disclosed that some teens create modified cigars called "blunts" by removing some or all of the core tobacco of a cigar and replacing it with marijuana.

"These findings are of profound concern and require our immediate action to inform the public about the health risks associated with cigar smoking," said HHS Inspector General June Gibbs Brown. "There is a great need for additional research on cigars, including prevalence, patterns of use, health effects, the addictive potential of cigars as well as the practice of blunting."

"There is no safe form of tobacco," said Surgeon General David Satcher. "We should require

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the same sort of warning labels on cigars that we already require on packages of cigarettes and spit tobacco. The absence of such a warning on cigars could lead consumers to erroneously conclude that cigars do not carry health risks."

Although sale of cigars to minors is illegal in all 50 states, the OIG report on "Federal and State Enforcement and Regulation" showed that state level enforcement is uneven and is generally given a lower priority than enforcement of unlawful cigarette and spit tobacco sales. Half the states, according to the study, are unaware of the ease with which minors can purchase cigars, the degree to which the use of cigars by minors is a problem, and the health risks caused by cigar smoking. OIG recommended that the government develop a public awareness campaign about the health effects of cigars.

The studies were requested by the Office on Smoking and Health at the Centers for Disease Control and Prevention. The request was triggered, in part, by new information showing surprisingly high use of cigars by minors and new scientific evidence from NCI that cigar use can cause cancers of the lungs, larynx, oral cavity and esophagus. Those results were contained in a NCI monograph, "Cigars: Health Effects and Trends," released in April 1998.

HHS has only recently begun to survey cigar use among young people, and the surveys have used different methodologies. Both CDC and the Substance Abuse and Mental Health Services Administration added questions about youth cigar use to their annual surveys for the first time in 1997. SAMSHA's National Household Survey on Drug Abuse, a written survey conducted in households, estimated that 5 percent of teenagers smoke cigars. CDC's Youth Risk Behavior survey, conducted in schools, estimated that 22 percent of youths have smoked a cigar in the past 30 days. These agencies have agreed that additional research will be required to better understand patterns of cigar use among young people.

In the focus groups conducted by the OIG, higher percentages of both male and female participants said they have smoked a cigar, with the highest use reported among urban teens. Fifty-four percent of the focus group participants had smoked a cigar sometime in their life, and of that number, two-thirds had done so in the past year, and more than one-third within the past 30 days. Of the 82 teens who had smoked a cigar in the past year, 60 percent also reported smoking cigarettes, while 16 percent reported having used spit tobacco products.

While most teens are first exposed to tobacco is through cigarettes, 22 percent of 159 focus group participants surveyed by the OIG, tried cigars first, again suggesting that more research is needed to determine whether cigars are attracting a new group of users who would otherwise not have used tobacco products.

Forty percent of the focus group participants reported that cigar use was increasing in popularity and use among their peers. About half of both suburban and urban participants said they expect to be using cigars in the next five years, despite general awareness of the health risks associated with smoking. The teens said that smoking cigars is more socially acceptable among teens and adults than smoking cigarettes or using spit tobacco. Moreover, they easily recalled a wide assortment of television shows, movies, and famous celebrities associated with cigar smoking.

Focus group participants said teens generally buy cigars at gas stations or convenience stores, typically smoke them at parties, frequently while drinking alcohol, and prefer manufactured cigars, to premium cigars, because of the ease of purchase, low cost, sweetened flavors and pleasant aromas. They further reported that many of their peers use cigars as "blunts" for smoking marijuana, especially in urban schools. While the practice is common at weekend parties, urban teens reported that blunting often occurs everyday. The report went on to say that cigars used as blunts for smoking marijuana are popular with teens because they reportedly result in a better high, improve the flavor of marijuana, and burn more slowly than cigarette paper.

The OIG report suggests that the ready availability of cigars to minors, and the increased popularity of cigars among teens, is partly due to the fact that cigars have not faced the same degree of regulation and oversight as other tobacco products. For example, the OIG report notes that no federal laws require cigar manufacturers to report their ingredients, and, aside from little cigars, they are not subject to television and radio advertising restrictions.

The only federal oversight for cigars is through a provision of the Public Health Service Act known as the Synar Amendment that requires states to conduct yearly, random, unannounced inspections of vendors to measure tobacco sales to minors.

Both studies are posted on the OIG Web site at http://www.hhs.gov/progorg/oig

Funding Opportunities:

NCI Offers Grant Supplements

Administrative Supplements To Study The Impact Of Cancer On The Family: The NCI Division of Cancer Control and Population Sciences announces the availability of one-time administrative supplements to NCI-funded Clinical and Comprehensive Cancer Center P30 awards to study the impact of cancer on the family. Budgets may not exceed $100,000 total direct costs for a time period not exceeding 12 months. The deadline for receipt of requests is May 14.

Inquiries: Michael Stefanek, DCCPS, NCI, Executive Plaza North Room 211, Bethesda, MD 20892-7381, phone 301-496-8776, fax 301-435-7547, email: ms496r@nih.gov

Administrative Supplements To Establish DNA Array Facilities: NCI announces the availability of administrative supplements to institutions with NCI-funded research projects to assist with purchase of equipment to establish DNA array facilities. The facilities must be designed to support application of these comprehensive molecular analysis technologies to innovative cancer research. A minimum of five NCI-funded research projects must be served by the activities of the array facility. Institutions with NCI-funded research project (R01), MERIT award (R37), program project (P01), Center Core (P30), Comprehensive Center (P60) or Specialized Center (P50) grants are eligible. The work proposed must be within the scope of the research originally approved by peer-review. Requests for supplements are limited to one per institution. Deadline for requests is May 5. NCI has set aside $2.5 million to support these supplements.

Inquires: James Jacobson, Division of Cancer Treatment and Diagnosis, NCI, 6130 Executive Blvd Room 700, Bethesda, MD 20892, phone 301-402-4185, fax 301-402-7819, email: jj37d@nih.gov

In Brief:

Foon To Direct Barrett Center; Hundahl Leads Commission

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University for his discoveries regarding the genetic basis of colon cancer. . . . **KENNETH FOON** was appointed director of Barrett Cancer Center at University Hospital and professor of medicine at the University of Cincinnati College of Medicine. For the past six years, Foon was directed the Lucille Parker Markey Cancer Center and chief of the Division of Hematology and Oncology at University of Kentucky in Lexington. . . . **SCOTT HUNDAHL**, a surgical oncologist from Honolulu, was elected chairman of the American College of Surgeons' Commission on Cancer during the College's annual Clinical Congress. Hundahl has been chief of surgery at the Queen's Medical Center in Honolulu since 1995. . . . **BRUCE STILLMAN**, director of Cold Spring Harbor Laboratory, was appointed an officer in the General Division of the Order of Australia, announced by the Governor-General of Australia. The appointment is made for distinguished service of a high degree to Australia or to humanity. Stillman, a native Australian, joined CSHL in 1979 and became director in 1994. . . . **J. TAYLOR WHARTON** of the University of Texas M. D. Anderson Cancer Center has been promoted to special assistant to the president and medical director of the new Cancer Consultant Program. Wharton was chairman of the Department of Gynecologic Oncology. He will coordinate a variety of patient relations activities as special assistant to the president. As medical director, Wharton will lead a new effort to address the growing demand by patients' for second opinions. . . . **AMERICAN CANCER SOCIETY** Pennsylvania Division has endorsed a proposal by NCI-recognized cancer centers that requests that 25 percent of Pennsylvania's tobacco settlement money be directed to cancer research. The settlement, approved by Philadelphia Common Pleas Court Judge John Herron, would send $11.3 billion to Pennsylvania over the next 25 years. The centers included in the proposal are Fox Chase Center, University of Pennsylvania Cancer Center, Kimmel Cancer Center at Thomas Jefferson University, The Wistar Institute, Temple University Cancer Center, Penn State Geisinger Cancer Center and University of Pittsburgh Cancer Institute. . . . **CANDACE JOHNSON** was named deputy director for basic research at University of Pittsburgh Cancer Institute. She has served as interim deputy director for a year. Johnson is a professor in the departments of pharmacology and medicine at the University of Pittsburgh School of Medicine, as well as co-director of the UPCI Experimental Therapeutics Program. . . . **DENNIS SLAMON**, director of the Revlon/UCLA Women's Cancer Research Program at the University of California, Los Angeles, Jonsson Cancer Center, received an Albert B. Sabin Heroes of Science award for the development of Herceptin. . . . **NCI DIVISION** of Cancer Control and Population Sciences is recruiting for a Health Scientist Administrator, GS-13/14, or a Medical Officer, GS13/14, in the Applied Sociocultural Research Branch. Information: phone 301-402-2789, or to receive information by fax, call 301-594-2953 or 800-728-5627 and enter fax ID #1905.

THE CANCER LETTER

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Business & Regulatory Report

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National Comprehensive Center Network, Quintiles Oncology, To Collaborate On Trials

Quintiles Oncology Therapeutics of Research Triangle Park, NC, and the National Comprehensive Cancer Network of Rockledge, PA, have signed a collaboration agreement granting Quintiles exclusive rights within the contract research industry to use and promote the central clinical research capabilities of NCCN, including the NCCN Outcomes Database.

The collaboration is designed to streamline the initiation and completion of clinical trials, and accelerate the development of the NCCN Outcomes Database, the NCCN and Quintiles said in a statement. The database contains aggregate information on the clinical outcomes,

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Oncology Management:

Tax-Exempt Bonds Issued To Expand UPCI; Sentillion, Duke Partner On Info System

UPMC Health System said it has issued $250 million in tax-exempt bonds that will be used partly to expand the University of Pittsburgh Cancer Institute through new building construction on the UPMC Shadyside campus.

The bonds were insured by Financial Security Assurance Inc., and are a triple A-rated investment. PNC Capital Markets served as the investment banker for the deal. The proceeds would also be used to finance construction of a new sports performance complex for UPMC's Center for Sports Medicine, information technology initiatives, and capital projects for the system and its subsidiary hospitals, officials said.

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Sentillion Inc. of Atlanta said it has entered into a partnership with Duke University Visual Integration Research Center, a multi-vendor initiative established to be an industry showcase for the use of visual integration standards and technology.

Other vendors involved in VIRC include Hewlett-Packard Medical Products Group, 3M Health Information Systems and Synthesys Technologies.

The partnership will use Sentillion's Context Management Engine to visually integrate Duke's multi-vendor information systems. The software includes "Patient Link," which enables disparate applications to automatically synchronize on the same patient, and "User Link," which provides clinicians with secure, single log-on access to these applications, the company said.

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NCCN, ACS Produce Guideline For Breast Cancer Patients

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procedures, and costs associated with cancer treatment.

"We believe this collaboration will result in faster study startup and provide better answers sooner about the efficacy and safety of new cancer treatments," said William McGivney, chief executive officer of NCCN.

NCCN includes 17 U.S. cancer centers.

Under the agreement, NCCN will develop centralized clinical research services, including an Institutional Review Board, legal and contracting services, and grant bid support. The agreement allows member institutions to choose whether to participate in the trials and use the services of the collaboration.

Quintiles will install and administer a central research data management system and investigator database, assist NCCN in developing central research administrative functions, and install the Quintiles "Collect Suite" of fax and Internet based data collection systems.

"Our alliance with NCCN will give our customers streamlined access to NCCN's premier academic medical centers and cancer researchers, and access to high-quality data in as close to real time as current technology allows," said Glenn Bilawsky, executive vice president of Quintiles.

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In another development, NCCN and the American Cancer Society have produced breast cancer treatment guidelines written for cancer patients and their families.

The guidelines were released at the NCCN annual meeting in Fort Lauderdale on March 1.

Among the topics covered are: types of breast cancer, stages of the disease, medical decisions and treatment options, important questions for patients to discuss with their doctors, general information about clinical trials, and a glossary of terms commonly used in breast cancer treatment.

The document also includes six flow chart algorithms that represent appropriate treatment for different stages of breast cancer.

"The NCCN Oncology Practice Guidelines, which now cover more than 95 percent of all cancer patients, have become the treatment standard for oncology professionals," said McGivney. "We are proud that our collaboration with the ACS will now bring these guidelines to the patients who need them the most."

"For more than 85 years, the public has relied on the American Cancer Society for accurate, up-to-date information about cancer and its treatment," said Charles McDonald, ACS president. "This joint effort with the NCCN ensures that breast cancer patients will have the information they need to better understand the disease and act, in conjunction with their physician, to get treatment that is right for them."

NCCN and ACS said they plan to translate other NCCN clinical guidelines into patient versions.

To obtain copies of the patient version of the breast cancer guidelines, contact NCCN at 1-888-909-NCCN or ACS at 1-800-ACS-2345, or on the Internet at http://www.nccn.org or http://www.cancer.org

Clinical Trials:

Phase I Trial Of Karenitecin Begins, BioNumerik Says

BioNumerik Pharmaceuticals Inc. of San Antonio has begun a phase I trial of karenitecin, and anticancer drug candidate. The first patient in the trial was recently treated at the University of Chicago Medical Center, the company said.

Karenitecin, a form of camptothecins, is the company's third drug candidate that has been brought from discovery to the clinic with the assistance of supercomputer simulations, the company said. The

preclinical development time for the three drugs has averaged 18 to 24 months, compared to the pharmaceutical industry average of six years, the company said.

Karenitecin has been designed to avoid problems with oral bioavailability, unfavorable metabolism, toxicity and drug resistance that have been associated with other camptothecins, the company said.

The drug candidate, which contains silicon, has demonstrated antitumor activity at concentrations as low as parts per trillion in laboratory testing with human cancer cell lines and in animals bearing human tumors, the company said.

"To engineer karenitecin, we simulated more than 12 trillion possible drug candidates using SGI/Cray supercomputing technology in less than one year, and it is clear that it would not be possible to discover and develop such a molecule without this technology operating in parallel with state-of-the-art laboratory research," Frederick Hausheer, a BioNumerik scientist, said in a statement.

The company said that in animal studies, orally administered karenitecin has demonstrated antitumor activity against common human solid tumors (including prostate, colon, breast, lung, melanoma and ovary) and potency against a variety of common human cancers, compared to existing camptothecin derivatives. The company said karenitecin has also demonstrated the ability to bypass common, tumor-mediated drug resistance mechanisms to which many other camptothecins appear to be susceptible. Since it is lipophilic, karenitecin may have enhanced tissue penetration, drug delivery and bioavailability, compared to existing water soluble camptothecins, the company said

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Celgene Corp. (Nasdaq: CELG) of Warren, NJ, announced a collaboration with the Radiation Treatment Oncology Group for the study of Thalomid (thalidomide), in conjunction with conventional surgery and radiation for the initial treatment of glioblastoma multiforme. The study will be conducted at 15 sites and will involve approximately 80 patients, the company said.

According to lead investigators, the protocol will include patients who have not previously undergone radiation therapy or chemotherapy. Following surgery, participants will be given thalidomide on the first day of their radiation treatment at a dose of 200 mg once daily. Thereafter, each patient's dose will increase every one to two weeks by 100-200 mg daily, to a maximum dose of 1200 mg daily, and will continue at that dose as long as no tumor progression or toxicity occurs. The study is expected to last for approximately two years.

Celgene has FDA clearance to market Thalomid for erythema nodosum leprosum in leprosy. The drug has been commercially available since last October. Last December, Celgene licensed from Entremed Inc. (Nasdaq: ENMD) the rights to thalidomide as an anti-angiogenic agent.

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Corixa Corp. (Nasdaq: CRXA) of Seattle, said it has begun a phase I trial of a microsphere-encapsulated Her-2/neu vaccine in breast, ovarian and lung cancer.

The vaccine is designed to stimulate T cells to destroy cancer cells. The biodegradable microspheres are composed of poly-lactic-polyglocolic acid, a synthetic co-polymer that has been approved by the FDA for use in sutures and certain pharmaceutical products, the company said.

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Enzon Inc. (Nasdaq: ENZN) of Piscataway, NJ, said **Schering-Plough Corp.** (NYSE:SGP) began phase III trials for combination therapy of PEG-Intron and Rebetol (ribavirin) for the treatment of hepatitis C.

PEG-Intron is a modified form of Schering's Intron A (interferon alfa-2b, recombinant) which was developed using Enzon's PEG technology.

Under the agreement between the two companies, Enzon is entitled to royalties for product sales and milestones, and has the option to exclusively manufacture PEG Intron in the U.S. Schering-Plough is continuing its development of PEG-Intron as a monotherapy for of hepatitis C. PEG-Intron is also in phase III trials for malignant melanoma and chronic myelogenous leukemia, as well as early stage trials for various solid tumors, the companies said.

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GLYCODesign, a privately-held company based in Toronto, said it plans to begin a phase I/II trial of oral GD0039, a chemoprotective agent, in advanced breast cancer patients receiving combination chemotherapy with 5-FU, doxorubicin and cyclophosphamide.

Trials are expected to begin in the spring of 1999 at the University of Chicago Medical Center, the company said. Gini Fleming, associate professor of medicine, will serve as the principal investigator at that site. The multicenter trial is expected to enroll

28 patients. The agent is being tested in Canadian phase II trials in renal cell carcinoma and colorectal cancer as an anti-cancer agent, the company said.

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ILEX Oncology Inc. (NASDAQ:ILXO) of San Antonio said it has initiated a phase III pivotal trial of eflornithine for the prevention of recurrence of superficial bladder cancer.

The NDA-directed trial is a double blind, placebo-controlled study of DFMO administered orally to patients with low-grade superficial bladder cancers after transurethral resection.

The study, co-chaired by Michael Sarosdy, of San Antonio, and Edward Messing, of Rochester, NY, will evaluate the chemopreventive efficacy of DFMO in 450 study participants at 39 clinical trial sites, the company said. The study, supported by NCI, is being conducted through the University of Wisconsin, Madison, and is scheduled to conclude in 2002.

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The Liposome Company (Nasdaq: LIPO) of Princeton, NJ, said it has begun a phase I trial of TLC ELL-12, a liposomal ether lipid, in advanced solid tumors, including non-small-cell lung, prostate and melanoma.

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MGI Pharma Inc. (Nasdaq: MOGN) of Minneapolis said it has begun to enrollment in a phase I study that will combine MGI 114, an anti-cancer drug, with CPT-11 (Camptosar), a drug used to treat colon and rectal cancer.

MGI 114 is the lead compound in MGI Pharma's category of agents called the acylfulvenes. The company said MGI 114 appears to have a unique mechanism of action; activity against tumor cell lines that are resistant to standard antitumor therapies; and a synergistic effect against tumor cells when combined with certain approved drugs. The company is conducting phase II trials in prostate, pancreatic and ovarian cancer.

Under an agreement with MGI Pharma, NCI has initiated a series of phase II trials that are planned to include at least two studies each in breast, colon, renal, ovarian and non-small cell lung cancer, and one study in cervical cancer, the company said. The Institute is also conducting a phase I study in pediatric cancer patients with solid tumors. CPT-11 is approved for metastatic cancer of the colon or rectum that recurs or progresses following treatment with 5-FU.

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NeXstar Pharmaceuticals Inc. (Nasdaq: NXTR) of Boulder, CO, began phase I trials of NX 211, a liposomal form of the investigational anticancer drug lurtotecan, a proprietary topoisomerase I inhibitor. The study will test the product in advanced stage solid tumors, the company said.

The trials are conducted in The Netherlands. Additional phase I studies are planned for Canada and the U.S. In Canada, the company's IND has been submitted and enrollment is expected to begin later this year, the company said. The IND to FDA is expected to be submitted during the first half of 1999, the company said.

NeXstar acquired lurtotecan under exclusive license from Glaxo Wellcome last May. Under the collaboration, NeXstar produced a liposomal formulation of lurtotecan, called NX 211.

NeXstar recently announced that it will separate its existing businesses, creating two independent, publicly-traded companies. One company, continuing under the NeXstar Pharmaceuticals Inc., will focus on oncology and infectious diseases, leveraging its core liposomal technology, its sales and marketing infrastructure and its drug development expertise for in-licensing late stage compounds. The other company, to be named Iterex Technologies Inc., will commercialize compound discovery technologies.

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ProScript Inc. of Cambridge, MA, said it has begun a second phase I trial of the proteasome inhibitor PS-341. The trial is being conducted at Memorial Sloan-Kettering Cancer Center under a company-sponsored IND. ProScript said it is also evaluating PS-341 in phase I trials at M.D. Anderson Cancer Center.

Approvals and Applications:

European Committee Signs Off On Paxene For KS Treatment

IVAX Corp. (Amex: IVX) of Miami, said the European Committee for Proprietary Medicinal Products has recommended approval of its paclitaxel drug Paxene for AIDS-related Kaposi's sarcoma.

Paxene was developed by Baker Norton Pharmaceuticals, IVAX's U.S.-based research and development subsidiary. The European approval will be held by Norton Healthcare Limited, its subsidiary in the United Kingdom.

"This approval provides a key entry for IVAX into the global oncology marketplace and adds impetus to our ongoing effort to develop and market an orally-

administered system for paclitaxel," said Phillip Frost, IVAX chairman and CEO. The company also has a NDA pending in the U.S. for a generic version of the Bristol-Myers Squibb drug Taxol.

Paxene is approved for KS in the US. However, its entry on the market has been blocked until expiration of the BMS market exclusivity under the Orphan Drug Act.

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Celsion Corp. (OTC BB: CELN) of Columbia, MD, said it has received approval of its Investigational Device Exemption application from FDA for its breast cancer treatment system which uses heat alone to ablate breast tumors and viable cancer cells. The IDE enables the company to begin a phase I trial at Massachusetts General Hospital.

The IDE approval enables Celsion to proceed with phase one clinical studies for its non-surgical, minimally-invasive system which utilizes focused heat alone to kill cancerous tumors in the breast, the company said.

Preclinical studies, using breast tissue-equivalent phantoms and tumors in live animals, verified that Celsion's system is capable of selectively heating tumors at temperatures of up to 46 degrees Celsius without damage to surrounding healthy tissues in the human breast, the company said.

Celsion's focused heat cancer treatment system previously received FDA Premarket Approval for commercialization as an adjunct to radiation therapy, the company said.

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Ligand Pharmaceuticals Inc. (Nasdaq: LGND) of San Diego, said FDA has granted marketing clearance for Panretin gel (alitretinoin) 0.1% for the topical treatment of cutaneous lesions of patients with AIDS-related Kaposi's sarcoma. Panretin gel is Ligand's first approved product and is the first topical therapy approved for KS, the company said.

Ligand said it will market Panretin gel in the U.S. with its already established specialty oncology and HIV-center sales force of 26 people.

Patients may apply Panretin gel to their KS skin lesions in the privacy of their homes twice a day or as instructed by their physicians

FDA clearance followed a review by its Oncologic Drugs Advisory Committee on Nov. 16, 1998.

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The Liposome Company (Nasdaq: LIPO) of Princeton, NJ, said FDA has accepted its NDA for Evacet, a liposomal formulation of doxorubicin.

The company said the drug has been shown to have antitumor activity equivalent to that of doxorubicin with reduced potential for cardiotoxicty. Data from three phase III trials of Evacet used as a first-line therapy for metastatic breast cancer, both alone and in combination with cyclophosphamide, show a statistically significant reduction in cardiotoxicity, as compared with doxorubicin alone and in combination with cyclophosphamide, the company said.

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R2 Technology Inc., of Los Altos, CA, said FDA approved two supplements for the company's ImageChecker M1000 System.

The first supplement covers a hardware upgrade to the processor unit that provides a substantial increase in throughput. The second supplement provides a significant improvement in the detection code resulting in a 30 percent reduction in extraneous markers while maintaining the same high sensitivity demonstrated in the originally improved device.

The ImageChecker is the first and only Computer Aided Detection System to receive FDA approval for use in breast cancer screening, the company said.

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Techniclone Corp. (Nasdaq: TCLN) of Tustin, CA, said the FDA Office of Orphan Products Development has given the orphan drug designation to the company's Tumor Necrosis Therapy for glioblastoma multiforme and anaplastic astrocytoma.

TNT, which binds to necrotic cells found in the core of solid tumors is in phase II trails in the U.S. for malignant glioma and a phase I/II trial for pancreatic, prostrate and liver cancer, the company said.

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U.S. Bioscience Inc. (AMEX: UBS) of West Conshohocken, PA, said its sNDA, submitted last December for the use of Ethyol(amifostine) to reduce the incidence and severity of radiation-induced xerostomia has been accepted for filing and granted priority review status by FDA.

FDA grants priority review status to drug products that, if approved, would be a significant improvement compared to marketed products. The review and action goal for priority review applications is six months from the date of submission.

The sNDA includes data from a phase III, open-label, prospective multi-center randomized trial

involving approximately 300 patients with head and neck cancer, the company said.

Ethyol is indicated to reduce the cumulative renal toxicity associated with repeated administration of cisplatin in patients with advanced ovarian or non-small cell lung cancer, and is marketed in the US by ALZA Corp. and co-promoted by U.S. Bioscience. Ethyol is marketed internationally by Schering-Plough Corp.

Patents:

Myriad Patents Spectrometry To Assess DNA Polymorphisms

Myriad Genetics Inc. (Nasdaq: MYGN) of Salt Lake City has been awarded US patent No. 5,869,242, for "Mass Spectrometry to Assess DNA Sequence Polymorphisms," the company said.

The patent covers the use of the mass spectrometer to detect mutations or other polymorphisms in nucleic acid samples. The mass spectrometer uses the ratio of molecular mass to charge of various molecules to identify them. Nucleic acids are made up of four different base molecules, each with a different mass to charge ratio.

By totaling the number of each of the four molecules in a sample and comparing it to a known standard, one can determine whether differences, or polymorphisms, exist in the sample.

The technology could eventually be used to replace the current industry standards of mutation detection by probe hybridization or by DNA sequencing using automated gel electrophoresis instruments, the company said.

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Corixa Corp. (Nasdaq: CRXA) of Seattle said the U.S. Patent and Trademark Office has issued a patent to Washington University in St. Louis, licensed exclusively worldwide to Corixa, for the breast cancer protein, mammaglobin.

The patent, No. 5,855,889, is entitled "Mammaglobin, A Secreted Mammary-Specific Breast Cancer Protein." The patents covers the mammaglobin protein and antibodies generated against it.

Mammaglobin is expressed in the adult mammary gland and has been shown to be differentially expressed in numerous breast carcinoma cell lines and in primary and metastatic human breast tumors, the company said. The breast-specific expression of mammaglobin and its marked over-expression in breast cancer specimens suggest that mammaglobin could potentially be used as a tumor vaccine antigen and as an effective marker for monitoring the clinical management of breast cancer, the company said. Further, detection of mammaglobin positive tumor cells may be useful as an in vivo diagnostic product or as an in vitro serum marker for breast carcinoma, the company said.

Mammaglobin refers to the novel gene and protein discovered by Mark Watson and Timothy Fleming both researchers at Washington University School of Medicine in St. Louis. DNA claims covering the mammaglobin sequence are the subject of previously issued US patents also licensed to Corixa, the company said.

Deals & Collaborations:

Firms Gets First Payment From Bristol-Myers For Taxol

Cytoclonal Pharmaceutics Inc. (Nasdaq: CYPH, CYPHW, CYPHZ) of Dallas said it has received its first payment of the year from Bristol-Myers Squibb under the agreement with the drug giant for the production of Taxol (paclitaxel). Last year, and BMS and Cytoclonal signed a license and research agreement for rights to fermentation production system and genes for Taxol, the companies said.

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Gensia Sicor Inc. (Nasdaq: GNSA) of Irvine, CA, said its wholly owned subsidiary, Gensia Sicor Pharmaceuticals Inc. has agreed to a strategic alliance with Abbott Laboratories (NYSE: ABT) for the marketing and distribution of Gensia Sicor's growing portfolio of oncology products.

The agreement will provide for the marketing and distribution throughout the U.S. of Gensia Sicor's current and future multi-source oncology products now under development. The financial terms of the agreement were not disclosed.

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Genzyme Molecular Oncology (Nasdaq: GZMO) of Framingham, MA announced the grant of a European patent covering p53 gene therapy and methods to detect loss of p53 function.

The p53 gene functions as a tumor suppressor gene which regulates cell growth. In more than 50 percent of human cancers, the p53 gene is functionally deficient.

The patent was granted to the Johns Hopkins

University and originated from the laboratory of Bert Vogelstein, at Johns Hopkins. Genzyme Molecular Oncology obtained certain therapeutic and diagnostic rights to the p53 gene through its 1997 acquisition of PharmaGenics Inc. a privately-held genomics company which had previously licensed these rights from the Johns Hopkins University. In turn, Genzyme Molecular Oncology licensed these p53 gene therapy rights to Schering-Plough Corporation in October 1998.

The grant of this patent triggers a $5 million milestone payment to Genzyme Molecular Oncology from Schering-Plough, the company said.

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ILEX Oncology Inc. (Nasdaq: ILXO) San Antonio, TX, and Eli Lilly and Company (NYSE: LLY) of said they have signed an agreement under which ILEX will develop the diarysulfonylurea, LY295501, a Lilly oncology compound.

Under the agreement, Lilly will have the option to further develop and commercialize the molecule after completion of certain unspecified clinical trials, the companies said. Should Lilly decide not to develop and commercialize the diarysulfonylurea, ILEX will have development and commercialization rights. ILEX will pay to Lilly milestone payments and royalties on sales in addition to a license fee. Lilly will make an undisclosed equity investment in ILEX Oncology.

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ImmunoGen Inc. (Nasdaq: IMGN) of Norwood, MA, said it has executed an agreement with SmithKline Beecham Plc (SB), London, (London Stock Exchange: SB)/ SmithKline Beecham, Philadelphia (NYSE: SBH) to develop and commercialize ImmunoGen's lead tumor activated prodrug, huC242-DM1.

Under the agreement, in addition to royalties, ImmunoGen could receive upfront cash and milestone payments totaling more than $40 million, the company said. At ImmunoGen's option, SB will purchase up to $5 million of ImmunoGen common stock over the next two years, subject to certain conditions.

SB will receive exclusive worldwide rights to commercialize huC242-DM1, except in certain Far East territories. SB and ImmunoGen will collaborate on the remaining development. ImmunoGen will have responsibility for the product's initial assessment in humans which is expected to begin in the second half of CY 1999.

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Medarex Inc. (Nasdaq: MEDX) of Annandale, NJ, said it has reacquired the worldwide rights to its MDX-210 anti-HER2 cancer product. Commercial rights to MDX-210 were previously held by Ciba-Geigy Ltd., which subsequently became part of Novartis. Novartis has elected not to participate further in the development of the product, Medarex officials said

"Several potential corporate partners have approached us about the MDX-210 product based upon the promising phase II results announced in late 1998," said Donald Drakeman, president of Medarex. "We will be exploring our partnering options as we move MDX-210 towards phase III trials."

MDX-210 is a bispecific antibody that targets the HER-2 receptor.

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NeoPharm Pharmaceuticals Inc. (AMEX: NEO) of Bannockburn, IL, and **Pharmacia & Upjohn Inc.** (NYSE:PNU) announced a definitive agreement for the development and commercialization of liposomal encapsulated paclitaxel and liposomal encapsulated doxorubicin, two of NeoPharm's cancer products.

The agreement includes an initial payment in excess of $15 million as well as milestone payments in excess of $50 million during the clinical development, the companies said. Also, Pharmacia & Upjohn will pay for all clinical and pre-marketing expenses associated with LEP and LED, the companies said. NeoPharm will also receive royalty payments overseas and a co-promotion profit split in the U.S.

Under the agreement, Pharmacia & Upjohn obtains exclusive worldwide rights to develop and market LEP and LED. The companies said they agreed to work together to identify and develop additional drugs in the Pharmacia & Upjohn's oncology portfolio using NeoPharm's liposome technology.

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Pharmaceutical Resources Inc. (NYSE: PRX), of Spring Valley, NY, said it has received FDA approval to market Hydroxyurea, the generic version of the Bristol Myers Squibb drug Hydrea.

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U.S. Bioscience Inc. (AMEX: UBS) of West Conshohocken, PA, said it signed a $20 million private placement agreement with investors lead by Domain Partners IV L.P., a health care venture capital fund and Proquest Investments L.P., an oncology focused venture capital fund.

The agreement calls for U.S. Bioscience to issue to the investors 2,686,728 shares of common stock at a price of $7.44 per share and warrants exercisable for three years, to purchase 537,346 additional shares of common stock at an exercise price of $11.17 per share, the company said.

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Warner-Lambert Co. (NYSE: WLA) of Morris Plains, NJ, announced a definitive agreement to acquire **Agouron Pharmaceuticals Inc.** (Nasdaq: AGPH) of La Jolla, CA).

The agreement is valued at approximately $2.1 billion, the companies said.

Agouron achieved total revenues of $467 million for the fiscal year ended June 30, 1998.

Oncology Management:

AOR Earns $30 Million, PRN Earns $29.8 Million

(Continued from page 1)

These applications allow clinicians to link charge capture with clinical results, and will soon be able to secure simultaneous entry to applications such as surgical scheduling, results reporting, coding compliance, clinical documentation and outcomes, the company said.

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American Oncology Resources Inc. (Nasdaq: AORI) of Houston earned $30.2 million ($0.61 per share) on revenues of $456 million for the year ended Dec. 31, the company said. Last year, the company's earnings were $22.9 million ($0.48 per share) and revenues $321.8 million.

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Physician Reliance Network Inc. (Nasdaq: PHYN) of Dallas earned $29.8 million ($0.56 per share) on revenues of $398 million for the year ended Dec. 31, the company said. Last year, the company lost $7.2 million ($0.14 per share) on revenues of $318 million.

Last December, AOR and PRN announced a definitive agreement to merge in a pooling of interest transaction. The transaction is expected to be completed in the second quarter of 1999.

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Response Oncology Inc.(Nasdaq:ROIX) of Memphis, TN, said it has terminated its Physician Practice Management contract with Knoxville Hematology/Oncology Associates.

The company said the practice was one of is three "underperforming physician practice management relationships."

Concurrently, the company said it has established a reserve against the three management agreements, which include a three-physician practice in Ft. Lauderdale, FL, and a three-physician practice in Tamarac, FL.

"The structure of these contracts has failed over time to align the physician and company incentives, producing deteriorating returns," Response Oncology said in a statement.

The company said it will take write-offs of $28 million to $32 million before taxes in the fourth quarter of fiscal 1998 "related to terminated development activities and reserves on certain accounts receivable."

The company said some of its earliest PPM acquisitions have underperformed due to the structure of these management agreements. According to the company, "these agreements do not spread the impact of the margin compression from the administration of certain new cancer drugs appropriately between the parties, resulting in a disproportionate burden on the company."

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Avandel Inc., a catastrophic care management company based in Lynnwood, WA, has launched a medical management program designed to reduce the cost, severity and frequency of catastrophic oncology events.

The program combines the medical management expertise of Quality Oncology, a national cancer disease management company, with the risk transfer capabilities of Avandel and its insurance partners.

Avandel's oncology management program will be integrated with the company's core Catastrophic Care Program, which includes specialized medical management services for specific catastrophic medical events, including organ and tissue transplants, medically compromised neonates, severe burns and severe injuries.

With the Catastrophic Care Program, clients will have access to Avandel Event Rates, which allow them to pay a fixed price for all medical costs associated with a catastrophic event.

Under Avandel's Catastrophic Oncology Management Program, only the most catastrophic tumor types including lung cancer, end stage breast cancer, colorectal cancer, leukemia, lymphoma and brain cancer will be managed.

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