THE CANCER LETTER INTERACTIVE

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

Vol. 25 No. 32
Aug. 13, 1999

FDA Can't Prohibit Distribution Of Articles, Books On Off-Label Drug Use, Judge Rules

The FDA Modernization Act violates the First Amendment by prohibiting drug companies from distributing peer-reviewed publications containing information on off-label use of drugs, a federal judge ruled last month.

The July 28 ruling by Judge Royce Lamberth, of the U.S. District Court for the District of Columbia, updates his earlier permanent injunction that struck down FDA laws and policies on distribution of peer-reviewed materials (**The Cancer Letter**, Aug. 14, 1998).

Lamberth's original ruling, last July, was viewed as a victory for

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In Brief:

NCI Awards 14 Contracts To Operate The Cancer Information Service

NCI CANCER INFORMATION SERVICE contracts have been awarded to 14 institutions to operate the 800-4-CANCER toll-free service. The five-year contracts, costing NCI a total of $20 million, take effect Oct. 15. The CIS regions, contractors, and their principal investigators, are:

New England—Yale University Cancer Center, New Haven, CT, **Vincent DeVita**;

New York—Memorial Sloan-Kettering Cancer Center, New York City, **Thomas Fahey**;

Atlantic—Fox Chase Cancer Center, Philadelphia, **Paul Engstrom**;

Mid-Atlantic—West Virginia University/Mary Babb Randolph Cancer Center, Morgantown, WVA, **Pamela Brown**;

Southeast—Duke University Cancer Center, Durham, NC, **Stephen George**;

Mid-South—University of Kentucky/Markey Cancer Center, Lexington, KY, **Thomas Tucker**;

Coastal—University of Miami Cancer Center, Miami, FL, **Edward Trapido**;

Midwest—Wayne State University/Karmanos Cancer Center, Detroit, **Vainutis Vaitkevicius**;

Heartland—University of Kansas Medical Center, Kansas City, **Stephen Russell**;

North Central—University of Wisconsin Cancer Center, Madison, **Patrick Remington**;

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FDA Can't Restrict Distribution Of Articles, Books, Court Says

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pharmaceutical companies, oncology professional societies, and several patient advocacy groups. However, four months after that ruling, FDAMA superceded several of the 1996 agency "guidance documents" Lamberth found unconstitutional. The agency then asked that the court to review the ruling in light of the new law.

"FDAMA largely perpetuates the policies held unconstitutional by the court, and therefore may not be applied or enforced by FDA," Lamberth wrote in the latest ruling.

"The government cannot justify a restriction of truthful, nonmisleading speech on the paternalistic assumption that such restriction is necessary to protect the listener from ignorantly or inadvertently misusing the information," Lamberth wrote. "[This] axiom is particularly powerful where the recipient of the information is a sophisticated listener trained extensively in the use of such information…"

The latest ruling covers the reprints of articles from peer-reviewed journals and chapters from textbooks. The ruling is expected to have its broadest impact in oncology, because oncologists frequently prescribe drugs off-label, experts said.

In the past, drug companies sought to distribute such materials to oncologists, but were stopped from doing do. The ruling does not explicitly cover abstracts from scientific meetings.

"It's a major decision," said Alan Bennett, an attorney with the Washington firm of Fox, Bennett & Turner. "It's squarely in the mainstream of constitutional law on commercial speech."

Bennett was involved in several disputes with FDA, stemming from attempts by his client, Bristol-Myers Squibb Co., to distribute peer-reviewed materials to oncologists.

The suit against FDA was brought by the Washington Legal Foundation, a public interest law and policy center. The action was filed on behalf of physicians who claimed that they were denied access to peer-reviewed materials distributed by drug companies.

Ruling Invalidates Key FDAMA Provision

Lamberth invalidated a key FDAMA requirement that pharmaceutical companies file supplemental NDAs within six months of starting to distribute peer-reviewed materials on off-label uses of drugs.

The requirement violates the First Amendment by making free speech contingent on submission of a regulatory application, Lamberth wrote.

As a legal matter, Congress and FDA had the authority to use a variety of mechanisms to encourage drug companies to submit SNDAs. However, "the government has not chosen to ban the prescription of drugs for off-label uses," the ruling states.

"It has not chosen to prohibit manufacturers from profiting from off-label prescriptions," the ruling continues. "It has not chosen to impose a fine or other pecuniary penalty on manufacturers for failure to seek supplemental applications, nor has it chosen to more stringently enforce its statutory authority to prosecute misbranding."

"Instead, Congress and [FDA] have chosen to condition the exercise of rights guaranteed by the US Constitution upon the submission of a supplemental drug application. Such a gross imposition upon free speech is in clear violation of the First Amendment, and cannot stand."

Under Lamberth's ruling, drug companies are allowed to distribute truthful materials that have appeared in peer-reviewed publications or medical textbooks. However, companies and their sales forces are apparently prohibited from editing, summarizing or characterizing the materials the materials they distribute, legal experts said to **The Cancer Letter**.

THE CANCER LETTER

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Subscription $275 per year worldwide. ISSN 0096-3917. Published 48 times a year by The Cancer Letter Inc.

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

"It bears repeating that there currently do exist numerous incentives for manufacturers to seek approval of off-label uses," Lamberth wrote in last week's ruling. "Manufacturers are still much more limited in their promotion of off-label uses than in the promotion of approved uses."

Lamberth's 1998 ruling rejected the FDA 1996 Guidance to Industry On Dissemination of Reprints of Certain Published, Original Data, as well as an earlier guidance document that covers the exchange of peer-reviewed information in the context of continuing medical education programs organized by "independent program providers."

The CME portion of the ruling was not challenge by FDA.

The ruling applies to distribution of unabridged articles published in "bona fide peer-reviewed journals" and portions of reference textbooks "published by bona fide independent publisher and otherwise generally available."

A bona fide peer-reviewed journal is defined as a "journal that uses experts to objectively review and select, reject, or provide comments about proposed articles." Reviewers should be independent from the journal and should have a demonstrated expertise in the subject of the article.

A bona fide independent publisher is defined as a publisher that has "no common ownership or other corporate affiliation with a pharmaceutical or medical device manufacturer and whose principal business is the publication of books through normal distribution channels."

The ruling does not explicitly mention abstracts published prior to scientific conferences.

"The word 'abstract' nowhere appears in the court's opinion," said Richard Samp, chief counsel of the Washington Legal Foundation.

"However, the court lay down certain First Amendment principles, and to the extent that a written work has the same indications of reliability that a peer-reviewed medical journal would have, then, presumably, the same First Amendment principles would prohibit FDA from trying to stop dissemination of those kinds of articles," Samp said to **The Cancer Letter**.

It is unlikely that the ruling would allow pharmaceutical companies to summarize the papers, Samp said. Such summaries are frequently printed directly on "reprint carriers," or files containing articles distributed to physicians.

"The text [on reprint carriers], clearly, is not covered and was not intended to be covered," Samp said. "The whole point of extending the First Amendment coverage to reprints of journals and the medical textbooks is that the manufacturer had nothing to do with writing the text, and therefore you have a pretty good bet that it is a reasonably balanced presentation. The moment you start talking about a text that was written by the manufacturer, FDA has a pretty good reason to fear that the text would not be at all balanced."

Sales reps distributing the papers would be precluded from offering summaries of the findings, Samp said.

"My understanding is that a salesman could walk into the office and could say to the doctor, 'Here is an article that appeared in last month's New England Journal of Medicine. It discusses an off-label of our drug XYZ. You might be interested in this.' A salesman can say what the off-label use is. But beyond doing that, it would not be proper to discuss the results of the study."

However, sales reps would be allowed to answer questions from physicians, Samp said. "If after reading the article the doctor said, 'That's interesting,' and has some follow-up questions, then the salesman could answer those questions."

Federal Science Programs:
NASA, NCI Explore Research On Sensor Technologies

NCI and the National Aeronautics and Space Administration have begun to collaborate on the development of technologies that would help NASA detect life on other planets and NCI detect cancer cells in humans, the directors of the two agencies said.

At the first of what is planned as series of NASA-NCI workshops, NASA Administrator Dan Goldin and NCI Director Richard Klausner said the goal of the new effort is to develop sensory and imaging machines that are part silicon chip, part biological systems.

"People think of the space program as rockets and combustion, but the space program is going to be about our understanding of biology," Goldin said. "Biological systems have the greatest untapped potential to revolutionize how we design, build and use future space systems. They are quite simply the most robust and efficient systems in the universe."

At the First NASA/NCI Workshop on Sensors

for Bio-Molecular Signatures, held June 2-4, at the Jet Propulsion Laboratory in Pasadena, CA, engineers and biologists participated in sessions on the recognition of bio-molecular signatures, micro/nano systems for sensing, molecular imaging, signal amplification, and information and data processing.

NCI Director Richard Klausner said that Goldin and he began talking about the two agencies developing these technologies together over the past year. "It goes back to some truly fantastic dinners, usually at [National Academy of Sciences president] Bruce Alberts' house, with Dan Goldin, where it was obvious as both of us were talking—generally at the same time—about where we needed to go, what problems we were struggling with, what technologies and new conceptualizations we were confronted with in terms of the missions of our agencies," Klausner said at the workshop.

"It was clear that there was a lot that we had in common and we ought to do together," Klausner said. "This workshop is part of a real commitment that the two of us have to do just that, and not only technology transfer, not only sharing some similar approaches, but figuring out how our traditionally distinct communities and constituencies could help work together and solve each other's problems and, in some ways change how each of us think about what we are trying to do."

Goldin, the NASA administrator since 1992, and Klausner, the NCI director since 1995, said each agency has funding programs that expect to support innovative technologies. NASA recently began the NASA Astrobiology Institute (http://nai.arc.nasa.gov), while NCI has begun its Unconventional Innovations Program (http://rcb.nci.nih.gov/uip.htm), a five-year, $48 million grant program to stimulate development of new technologies in cancer care.

"[NASA and NCI] both need to develop nano-scale sensors with sensitivities and detection capabilities at the molecular level, and we need to transmit the information we acquire to other systems outside the body or inside our spacecraft," Goldin said.

Goldin's "Fantasy Trip"

To illustrate how NASA hopes to use these technologies, Goldin described a "brief fantasy trip in the future," circa 2030, of an interstellar probe that would search for life in other solar systems:

"The Coke can-sized spacecraft will reach and land on a passing asteroid two years after it is launched from Earth," Goldin said, as if reading from a future NASA press release. "Aboard the asteroid, the spacecraft will use its DNA-based biomimetic system as a blueprint to evolve, adapt and grow into a more complex exploring and thinking system. It will ride the asteroid like a parasite until it transforms itself into its next evolvable state—an intelligent interstellar probe."

This imagined spacecraft would use the asteroid's iron, carbon, and other materials to build its structure, nervous system, and communications, Goldin said. "Such a spacecraft sounds like an ambitious dream, but it could be possible if we effectively utilize biologically-inspired technologies," Goldin said.

"The greatest attribute that biological systems have over solid state systems is the ability to change on their own," Goldin said. "This could be to adapt to different operating environments, to accomplish different tasks, or to renew and repair themselves.

"A system shouldn't walk off a cliff simply because someone in Mission Control sent it forward 10 paces, or miss looking at a strange bluish liquid just because we pointed it toward a rock."

Similarly, tiny versions of these devices could perform diagnostic and monitoring functions in humans, or to control drug delivery, Goldin said. "We can put nano-scale probes in the body to look for specific bio-chemical structures, we can characterize what we find categorize and count them, model them and report the results."

The full text of Goldin's remarks at the workshop are available at ftp://ftp.hq.nasa.gov/pub/pao/Goldin/1999/biomolec.html

Goal To Detect Cancer As Early As Possible

Klausner discussed NCI's effort to support research and technology that will enable the molecular diagnosis of cancer and specific classification of cancer type according to molecular characteristics.

"The central challenge and goal of cancer biology now is to be able to read and interpret genetic molecular changes in order to detect cancer as early as possible," Klausner said. "We want to move to a point where we don't ever want to wait to detect cancer, where there are dozens of changes, but actually detect pre-cancer. We want to be able to read the collection of changes, because it is the specific collection of informational changes that defines the actual nature of each disease….

"We can imagine core technologies of molecular-scale machines that have multifunction sensing capacity, because its almost undoubtedly going to be patterns of changes that we are going to be looking for," Klausner said. "We need these sensors to be capable of generating signals based upon the fact that they have recognized something. We need this information to be communicated and analyzed.

"Then we would love to be able to use that decision point to initiate intervention by interacting these molecular machines with externally applied radiation, for example," he said.

NCI's Unconventional Innovations Program is designed to support "high-impact, long range developments through investments in novel technologies or quantum improvements in existing technologies," Klausner said.

"We need to build technology platforms integrating non-intrusive sensing of cancer profiles in the living body, transmission of information to an external monitor, controlled intervention specific for the cancer profile, and monitoring of the intervention," he said.

The first $4 million of these grants will be funded next month, and the Institute plans to commit another $44 million through fiscal 2003, Klausner said. "If we do well with appropriations, this is a program we think should have more than that," he said.

In addition to the Unconventional Innovations Program, Klausner described the following projects:

—NCI's Cancer Genome Anatomy Program has the goal of finding every human gene and determining the changes in the genes. The Institute is beginning to identify the signatures of cancers. For example, one project has identified 18,000 genes involved in diffuse large cell lymphoma. All this information is on a silicon chip, which can be used to compare patients with identical diagnoses to determine whether the diseases are, in fact, identical.

—NCI plans to spend $50 million over the next five years to fund research to develop molecular classification schemes for all human cancers. This project is called the "NCI Director's Challenge."

"We really are convinced that the type of problems we've laid out here are going to be hard, but they really ought to be solvable," Klausner said. "We are committing to using whatever resources we have to find new mechanisms to fund and develop the programs that will take us from where we are to where we must be and get there quickly."

A Need For Training, Sustained Support

At the workshop, Roger Brent, associate director of the Molecular Sciences Institute at University of California, Berkeley, said funding for this type of research would need to be sustained over many years in order to train more scientists in this emerging field.

"The development of biological technology is a wonderful thing, and it will enable many things, including health care and the space program, take concepts from life and turn them into half-biological half-silicon machines," Brent said. "But biological technology is really hard to do well. The number of people with the skill set to know about biological entities and take use them for engineering things is really very small.

"If we are going to go this way we are going to have to bring in a community of younger people," Brent said. "Then you can't let them down—if you are in it for the long haul—by playing games with the funding."

Brent described the work of his team at Berkeley in developing, over the next 10 years, "a machine that help us measure what proteins are expressed in the cell and their association state—who are they complex with who are they talking with—and their modification state, are they phosphorylated or not."

Brent said a machine also will be needed to answer the following questions: "What receptors are on the membrane, are they bound or not, and if so, by what? What proteins are in the nucleus and cytoplasm, what are their modification states, and what are their interaction states? What sites on the DNA are bound and by what?

"If we had a machine that could deliver each of those three things, we might not say we could understand biology, but I am confident we could make good decisions about therapy," Brent said.

Most of the workshop presentations are posted at http://cism.jpl.nasa.gov/events/workshops/nasa-nciagenda.html.

The Cancer Letter Takes Annual Publication Break

The Cancer Letter will not be published for the next two weeks while the staff takes its annual summer break. The next issue, Vol. 25, No. 33, will be published Sept. 3. The customer service office remains open at 800-513-7042.

NCI Reports On Prevention Among Native Americans

NCI has released a monograph that summarizes the Institute's first nationwide effort to address the cancer prevention and control needs of the Native American population.

The report, called "Native Outreach: A Report to American Indian, Alaska Native, and Native Hawaiian Communities," presents the results of seven research studies conducted in Native American communities.

According to data collected between 1988 and 1992, the highest cancer incidence among American Indian (New Mexico), Alaska Native and Hawaiian women was breast cancer. American Indian women had higher incidence rates for cancers of the cervix, ovary, and gallbladder than the U.S. white female population, and cervical cancer incidence among Alaska Native women was twice that of the U.S. white population. The leading cause of cancer cases and deaths among Alaska Native and Hawaiian men was lung cancer, while prostate cancer was the leading cause of cancer cases and deaths among American Indian men.

The monograph documents findings from seven of eight Native American studies funded by NCI between 1989 and 1996. There were two kinds of studies: identifying ways to prevent cancer deaths in Native American populations and finding ways to prevent cancer in these populations.

The monograph is written for community leaders, health professionals, and lay health workers to provide models for programs that can be implemented at a community level. Copies of the report (NIH Publication 98-4341) and an executive summary (NIH Publication 99-4341S) are available from NCI's Cancer Information Service at 800-4-CANCER (1-800-422-6237).

NIH News:

NCI Nominates Herbal Products For Toxicity Testing By NTP

Four herbal products—aloe vera, ginseng, kava kava and milk thistle—and a substance in vegetables thought to inhibit cancer have been recommended by a panel representing the federal health agencies for toxicity testing under the National Toxicology Program at the National Institute of Environmental Health Sciences.

Program officials said that NCI nominated all five for testing because of their widespread or increasing use by the public. The officials said the substances were then reviewed and approved by the federal Interagency Committee for Chemical Evaluation and Coordination, which advises NTP's testing. Such recommendations are often made when the popularity of a relatively untested substance exposes large numbers of people. No data indicating a known problem is required for a nomination.

Before making a final decision to test the substances, NTP is requesting public comment and any additional scientific information be sent to Dr. William Eastin, NIEHS/NTP, Box 12233, Research Triangle Park, NC 27709, or email at Eastin@niehs.nih.gov by Sept. 7.

The four herbs are aloe vera, which is used as a dietary supplement as well as a cosmetic; ginseng, which is promoted for vigor; kava kava is used as a mood elevator, and milk thistle, is considered by some to have anti-cancer and liver-protective properties. The fifth nomination is for indole-3-carbinol, a substance in cruciferous vegetables such as broccoli, and thought to have potential to reduce the risk of cancer.

NIEHS said that the current toxicity information on the substances is considered "inadequate."

A formal announcement of the request for comment is in the "Federal Register" vol. 64, no. 129, pp. 36704-36707.

NIDDK Funds Clinical Centers For Hepatitis C Research

The National Institute for Diabetes, Digestive and Kidney Diseases has awarded $28 million to fund an 8-year clinical trial of anti-viral drugs on treatment for chronic hepatitis C.

The study will test whether long-term treatment with these drugs can slow or prevent the progression of liver disease in HCV patients. Some HCV patients develop cirrhosis or liver cancer.

NIDDK will fund nine centers around the U.S., a virology laboratory, and a data coordinating center. The trial will recruit patients with chronic HCV who have previously been treated with alpha interferon but who could not sustain reduced enzyme and virus levels. Recruitment is tentatively scheduled to begin early next year. Researchers will decide which drugs will be used and the number of volunteers to be recruited this summer.

The principal investigators of the trial are:

Herbert Bonkovsky, University of Massachusetts Medical School; Adria Di Bisceglie, St. Louis University; Jules Dienstag, Massachusetts General Hospital; Gregory Everson, University of Colorado Health Sciences Center; John Hoefs, University of California, Irvine; William Lee, University of Texas Southwestern Medical Center; Karen Lindsay, University of Southern California; Anna Lok, University of Michigan; Mitchell Shiffman, Virginia Commonwealth University.

The Virology Laboratory will be operated by David Gretch, University of Washington, and the Data Coordinating Center by Elizabeth Wright, New England Research Institute.

Funding Opportunities:

NCI Program Announcement

Stages of Breast Development: Normal to Metastatic Disease

This initiative solicits investigator-initiated research grant applications addressing biological issues considered critical for progress in combating breast cancer. The purpose is to encourage new projects focusing on the biology that underlies the development and maturation of the normal mammary gland and alterations involved in early malignant and metastatic breast cancer. Multidisciplinary collaborations between, for example, cell biologists, molecular endocrinologists, bioengineers, geneticists, and mammary pathologist, are encouraged.

It is expected that a complete understanding of mammary gland development will form critical underpinnings for continued advances in detecting, preventing and treating breast cancer. Much of our biological research in breast cancer has focused on understanding the initiation and development of the disease. It is now recognized that an increased knowledge base in normal breast development, the earliest breast lesions leading to invasive cancer, and how breast cancer spreads throughout the body would greatly aid our understanding of this disease.

Inquiries: Barbara Spalholz, Ph.D., Cancer Cell Biology Branch, NCI Division of Cancer Biology, phone 301-496-7028, email: bs62d@nih.gov

NCI Contract Award

Title: Cancer Therapy Evaluation Program Informatics and Computer Support.

Contractor: Capital Technology Information Services, Rockville, MD; $21,867,137.

In Brief:

NCI Awards 14 CIS Contracts; ACS Names Two New VPs

(Continued from page 1)

South Central—M.D. Anderson Cancer Center, Houston, **Stephen Stuyck**;

Rocky Mountain—Penrose-St. Francis Health Systems, Colorado Springs, CO, **Donna Bertram**;

Pacific—Fred Hutchinson Cancer Research Center, Seattle, **Leland Hartwell**;

California—Northern California Cancer Center, Union City, CA, **Dee West**.

The new awards represent a consolidation of 19 CIS regions into the 14 listed, in response to a report on CIS last year by the General Accounting Office. Some of the contractors will be partnering with other institutions in their regions. The GAO report also called for upgraded equipment and information that would enable CIS contractors to serve more callers and result in fewer busy signals.

* * *

DANIEL SMITH was named national vice president of federal and state government affairs for the American Cancer Society. Smith most recently served as staff director for the Senate Committee on Agriculture, Nutrition and Forestry. Previously, he served as chief of staff to Sen. Tom Harkin (D-IA). . . . **A. GREGORY DONALDSON** was appointed national vice president of corporate communications for the American Cancer Society. Donaldson was senior director of corporate communications and senior corporate spokesman for Humana Inc. in Louisville, KY. . . . **JOHN DURANT**, executive vice president of the American Society of Clinical Oncology, received the 1999 Distinguished Southern Oncologist Award, the highest honor bestowed on an oncologist by the Southern Association for Oncology. Durant received the award Aug. 6 at the SAO annual assembly in Bermuda. The award recognized Durant's outstanding contributions to the advancement of medicine in the field of oncology. . . **ARTHUR SCHATZKIN** was named chief of the Nutritional Epidemiology Branch in the NCI Division of Cancer Epidemiology and Genetics. Schatzkin has been an investigator in the branch since 1997. He joined NCI in 1984 as a senior staff fellow in the Cancer Prevention Studies Branch, NCI Division of Cancer Prevention and Control, becoming a senior investigator in 1988. Schatzkin received a B.A. from Yale University, an M.D. from the State University

of New York, and an M.P.H. and Dr.P.H. from Columbia University. . . . **JULIA HOWE ROWLAND** has been named director of the NCI Office of Cancer Survivorship, succeeding **Anna Meadows**. Rowland served as an associate professor and director of the psycho-oncology program at Georgetown University School of Medicine. . . . **ROBERT HOOVER**, director of the NCI Epidemiology and Biostatistics Program, was presented the Distinguished Service Award by DES Action USA, a non-profit organization. Hoover was honored for his dedication to research benefiting DES-exposed individuals. . . . **NCI ALL IRELAND** Cancer Conference, sponsored by NCI and the departments of health of Northern Ireland and the Republic of Ireland, is scheduled for Oct. 3-6, in Belfast, Northern Ireland. The conference will mark the beginning of a long-term initiative to enhance cancer research in Ireland, the organizers said. Featured speakers at the conference will include NIH Director **Harold Varmus**, NCI Director **Richard Klausner**, NCI Division of Clinical Science Director **Edison Liu**, NCI Surgery Branch Chief **Steven Rosenberg**, NCI Radiation Oncology Branch Chief **Norman Coleman**, as well as **Henrietta Campbell**, chief medical officer, Northern Ireland; **James Kiely**, chief medical officer, Republic of Ireland; **Peter Daly**, associate professor of oncology, St. James's Hospital, Dublin; and **Patrick Johnston**, professor of oncology, Belfast City Trust Hospital. Registration information may be found at http://www.allirelandcancer.com or phone 888-624-1937. . . . **HELENA CHANG**, director of the Revlon/UCLA Breast Center at the University of California, Los Angeles, Jonsson Cancer Center, received a 1999 Leadership Award from Leadership Education for Asian Pacifics Inc. . . . **CAPITOL ASSOCIATES INC.**, a government relations firm specializing in health and based in Washington, DC, has hired two associates: **Lizbet Boroughs** and **Matthew Williams**. Boroughs was director of legislative affairs for the National Mental Health Association. Williams was assistant director of government relations for the Georgia Hospital Association. . . . **AMERICAN HOSPITAL** Association and the Biotechnology Industry Organization have signed a memorandum of understanding to work together on public policy initiatives related to new technologies and treatments, educational programs, and media activities. . . . **CANCER CARE INC.** recently bestowed four annual awards. **Wayne Yetter**, president and CEO of Novartis Pharmaceuticals Corp., received the Human Services Award, for leadership for the benefit of people with cancer. **Lynne Ronon**, senior vice president and GMM of Saks Fifth Avenue received the Fashion Leadership Award, recognizing fashion industry figures. **Amy Spindler**, Style editor of The New York Times Magazine, was awarded the Beacon Award, and author **Anna Quindlen** received the Regulus Award. . . . **AMERICAN CANCER SOCIETY** and Jones and Bartlett Publishers, of Sudbury, MA, have announced a partnership to provide cancer drug information to the public via the ACS website (http://www.cancer.org) as well as through a new publication, Consumer's Guide to Cancer Drugs. Under the agreement, J&B also will provide cancer drug information to the ACS information phone line, 800-ACS-2345. . . . **W.M. KECK FOUNDATION** of Los Angeles announced the recipients of its 1999 Distinguished Young Scholars in Medical Research program. Each recipient will receive $1 million to support research over the next five years. The winners were: **Bruce Clurman**, of Fred Hutchinson Cancer Research Center; **Judith Frydman**, of Stanford University; **Mark Gerstein**, of Yale University; **Partho Ghosh**, of University of California, San Diego; and **Phyllis Hanson**, of Washington University, St. Louis. . . . **FRANZ CANCER** Research Center, of Portland, OR, received a $1 million gift to be applied toward the construction of the Human Applications Laboratories. Construction is expected to be completed next month. The center is part of the Providence Portland Medical Center. . . . **THE BRAIN TUMOR FOUNDATION**, dedicated to the provision of social and psychological support to patients and families, has been formed. **Patrick Kelly**, professor and chairman of neurosurgery at the New York University School of Medicine, is the founder and president of the organization. Members of the foundation's Scientific Committee are: **Armando Basso**, of Bueno Aires; **Giovanni Broggi**, of Istituto Nazionale Neurologica, Milan, Italy; **Peter Burger**, of Johns Hopkins Medical Institutions; **J.P. Chodkiewicz** and **Catherine Daumas-Duport**, both of Centre Hospitalier St. Anne, Paris; **Bernadine Donohue**, NYU Medical Center; **E. Tessa Hedley-Whyte** and **Jay Loeffler**, both of Massachusetts General Hospital; **Christoph Ostertag**, of Neurochir University Klinik, Freiburg, Germany; **Steven Rosenberg**, of NCI; and **David Thomas**, of Institute of Neurology, London.

THE CANCER LETTER

Vol. 14 No. 8
August 1999

Business & Regulatory Report

Formerly "Cancer Economics"

Oncology Management:

Response Oncology Closes Six Centers Due To Fewer Bone Marrow Transplants

Response Oncology Inc. (Nasdaq: ROIX) of Memphis, TN, said it has closed six of its 53 transplant centers and plans to close an additional four over the next quarter.

In a statement, the company said "business has slowed" down after the release of the results of NCI-sponsored studies of bone marrow transplantation of breast cancer. The data were released last May.

As a result, Response Oncology said the number of bone marrow transplants in the second quarter dropped to 256, from last year's second quarter level of 333. Response Oncology said it decided to close the centers because "patient volume in these centers had fallen below the company's

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Clinical Trials:

FDA Gives EntreMed Permission To Begin Endostatin Trials, IRB Review In Progress

EntreMed Inc. (Nasdaq: ENMD) of Rockville, MD, said it has been notified by FDA that "permission has been granted for the Endostatin protein clinical trials to begin." EntreMed's Investigational New Drug application for Endostatin protein was submitted to FDA on June 24.

The company said it has a sufficient quantity of the Endostatin protein manufactured to GMP standards and vialed for human testing. EntreMed said it is obtaining the approvals from the Institutional Review Boards at each of the clinical trial sites.

The first phase I trial will be conducted at Dana-Farber/Partners CancerCare, the joint-venture between Dana-Farber Cancer Institute, Brigham and Women's, and Massachusetts General Hospitals. Two additional phase I sites, sponsored by the NCI, are the University of Texas M.D. Anderson Medical Center, and the University of Wisconsin Comprehensive Cancer Center.

* * *

Celgene Corp. (Nasdaq: CELG) of Warren, NJ, announced the initiation of a randomized, placebo controlled, phase II trial by the intramural Division of Clinical Sciences at NCI to administer Thalomid (thalidomide) or placebo to 94 patients following surgical resection of metastases from colon and rectal carcinoma.

The study will be conducted at the Warren Magnuson Clinical Center at NIH. A primary objective is to determine the time to recurrence for

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Decline In Transplants Hits Response Oncology

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quality assurance standards."

"The company expects that the decline in procedures will adversely affect profitability in the second and third quarters," the statement read. "The financial impact associated with this loss of business has been mitigated somewhat by the closing of certain centers and the reduction of some of the associated corporate overhead.

"We believe that the study findings released by ASCO and NCI, with additional maturation, will result in improved treatment strategies and refined patient selection criteria," said William West, chairman of Response Oncology. "The role of high dose chemotherapy remains well defined for several important hematologic malignancies, including recurrent lymphoma and multiple myeloma. We are convinced that high dose chemotherapy remains an important platform for certain women with breast cancer. Improved outcomes for these patients will require more effective strategies for minimal residual disease. We will devote considerable energy to a rapid definition of promising maintenance regimens."

The company said it has recently developed new high dose chemotherapy protocols that involve "monoclonal antibodies and oral chemotherapy drugs."

THE CANCER LETTER

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Publisher: Kirsten Boyd Goldberg
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Business & Regulatory Report (formerly Cancer Economics) is published 12 times a year as a supplement to The Cancer Letter. ISSN 1053-9611.

These studies involving the use of high dose chemotherapy sparked controversy among oncologists, and, in the aggregate, caused confusion among patients and physicians about the role of high dose chemotherapy in the treatment of breast cancer.

The company said its PPM business, which remains its largest business segment, continues to grow, "helping to offset some of the untoward consequences of this transitional period in the high dose chemotherapy program."

In a related development, Joseph Clark, president, CEO, and director of Response Oncology resigned "to pursue his personal entrepreneurial interests." In the interim, company chairman West will step in as president and CEO.

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AstraZeneca Plc. of London said it is conducting a "strategic and operational review" of its cancer care delivery and agrochemicals businesses, the company said in its six-month report. Analysts widely attributed the language of the statement as an indication of the company's intent to get out of the cancer care and fertilizer businesses.

"A full strategic review of the Salick Health Care business is being undertaken in light of the pressures on the profitability of the U.S. health care service sector and the prospect of further tightening of regulations," the company said in a press release.

Earlier this summer, AstraZeneca conducted a purge of Salick's top management, replacing oncologist CEO Lawrence Piro with attorney business executive Peter Jessup (**The Cancer Letter Business & Regulatory Report**, July).

The shakeup at Salick's Los Angeles headquarters was aimed at achieving a less top-heavy regulatory structure, the company said at the time. Several observers and insiders said the move also reflects the company's abandonment of plans to expand the Salick business, by giving greater autonomy to the cancer centers.

The move toward autonomy has its limits since the company has to finance its $50 million-plus investment in the highly competitive New York market, where AstraZeneca is about to open a cancer center at St. Vincent's Hospital. That project has been plagued with delays and cost overruns, insiders said.

Saddled with the burden of the St. Vincent's venture, the company has eliminated ist dialysis business and abandoned plans to expand in the Philadelphia market by letting the clock run out on a deal with Temple University. In California, the

company abandoned plans to develop a transplantation business and shut the doors of the Van Nuys Breast Center.

According to the Aug. 10 issue of Disease Management News, an industry newsletter, Salick has been phasing out of the cancer disease management business. Recently, the company changed its risk-based contract with CIGNA HealthCare in Arizona to a case management arrangement. Similarly, the company has retreated from the risk-based cancer care business in Florida. Its contracts with Physician Corp. of America and a Humana health plan are now gone, Disease Management News reported.

According to the AstraZeneca statement, Salick lost $4 million on revenues of $118 million during the first six months of 1999. Last year, the company lost $3 million on revenues of $102 million.

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Cardinal Health Inc. (NYSE: CAH) of Dublin, OH, announced two exclusive, five-year agreements with **US Oncology Inc.** (Nasdaq: USON) of Houston. The companies said that under the agreements, U.S. Oncology would purchase more than $2.5 billion of pharmaceuticals, medical supplies and automated dispensing and inventory-management systems from two Cardinal companies.

US Oncology made the deals with **Pyxis Corp.**, a developer and provider of automated dispensing and inventory-management systems, and **National Specialty Services Inc.**, a distributor of pharmaceuticals, medical supplies and other health care products to physician practices, home care companies and other sites of patient care outside hospitals.

The Pyxis system, trade name Pixisstation, would connect each US Oncology treatment center with National Specialty Services, said Tom Bang, Pixis president, new markets. The system would help manage inventory and streamline the order-entry process, Bang said.

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US Oncology earned $17.8 million, excluding the costs of a merger, on revenues of $266.4 million for the second quarter ended June 30. With merger costs included, the company posted a loss of $1.2 million.

The company was created June 15 by the merger of American Oncology Resources Inc. and Physician Reliance Network Inc. During the second quarter of 1998, PRN and AOR together earned $15.5 million on revenues of $204.7 million.

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ICSL Clinical Studies, a division of Innovative Clinical Solutions Ltd. (Nasdaq: ICSL) of Providence, RI, and **Tenet Healthcare Corp.** (NYSE: THC) of Santa Barbara, CA, said they have agreed to expand trials of cancer drugs at Tenet hospitals.

In the initial phase of the agreement, ICSL will develop research partnerships with a minimum of eight oncology departments at Tenet hospitals as part of the ICSL Oncology Research Network. Financial terms of the agreement were not disclosed.

ICSL Clinical Studies will work with each of the Tenet facilities to create the infrastructure required to conduct quality clinical research and disease management programs. Also, ICSL will provide and train employees at each Tenet location, and will provide central management functions through its Site Support Services office in Providence, RI. SSS includes business development, budgeting and contracting, regulatory coordination, patient recruitment, project management, information systems, quality assurance, training and education, and financial services.

The Oncology Research Network is a division of ICSL Clinical Studies that integrates clinical research within medical oncology practices. The addition of the Tenet physician practices brings the total number of medical oncologists within the Oncology Research Network to more than 100 with 17 research locations, and expands the network's reach to include the West Coast and in the southeast and southwest. Since its inception in 1998, the Oncology Research Network has initiated more than 50, multi-site trials.

Tenet owns and operates 130 acute care hospitals with more than 30,000 beds and numerous related health care services.

Clinical Trials:

NCI Begins Phase II Trial Of Thalomid For Colon Cancer

(Continued from page 1)

patients receiving surgical resection plus Thalomid treatment for metastatic colorectal disease, compared to patients receiving resection plus placebo. The study is also intended to measure the antiangiogenic activity in the patients receiving Thalomid.

The Thalomid study group will be treated for 24 months.

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EDAP TMS S.A. (Nasdaq: EDAPY and EASDAQ: EDAP), of Vaulx-en-Velin, France, said **Georgetown University** has conducted the first prostate cancer treatment in the U.S. using the Ablatherm, EDAP's minimally invasive device which utilizes the company's proprietary High Intensity Focused Ultrasound (HIFU) technology for the treatment of localized prostate cancer.

"Ablatherm holds great promise as a method to treat localized prostate cancer with a minimum of side effects," John Lynch, Chief of Urology at Georgetown University Medical Center.

The trial is being conducted under an Investigational Device Exemption granted to EDAP by FDA last January. Georgetown is the first of three U.S. sites to treat patients in the IDE study, which is slated to include 120 prostate cancer patients who have already been treated with radiation but experienced a recurrence. The other sites included in the trials are Baylor University and the University of California at San Francisco.

The minimally-invasive technology utilizes a focused ultrasound beam which quickly generates high-temperatures in precise volumes to destroy tumors without affecting the surrounding tissue, the company said.

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IDEC Pharmaceuticals (Nasdaq: IDPH) of San Diego said it has entered into a Clinical Trials Agreement with the NCI Division of Cancer Treatment and Diagnosis.

The focus of the agreement is the clinical study of the safety and efficacy of Zevalin (ibritumomab tiuxetan), formerly known as IDEC-Y2B8. The company's investigational, yttrium-based radioimmunotherapy will be explored as treatment for conditions outside those currently under investigation by IDEC. The company is conducting two pivotal clinical trials in non-Hodgkin's lymphoma, both of which are in advanced stages of patient accrual, the company said.

"This collaboration with the NCI will allow us to explore additional population treatment regimens where Zevalin could potentially benefit patients with hematologic malignancies," said Christine White, senior director, clinical oncology and hematology at IDEC. "These will include investigational studies in intermediate and high-grade NHL, as well as extensive bone marrow involvement [in patients] who have been ineligible for IDEC's pivotal studies. Other areas for clinical research could include combination therapy with chemotherapy and re-treatment of patients."

Zevalin is a monoclonal antibody attached to a linker, which chelates the radioisotope, yttrium-90. The antibody targets the CD20 antigen on mature B-cells, enabling Zevalin to deliver radioactivity to B-cell tumors throughout the body. Since NHL can involve bone marrow where blood cells are formed, there can be some radiation received by these normal cells.

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LifeCell Corp. (Nasdaq:LIFC) of The Woodlands, TX, announced the initiation of a collaborative study with Pharmacia & Upjohn (NYSE:PNU) and the M. D. Anderson Cancer Center. The nine-month study, funded in part by the U.S. Navy, is one of several ongoing evaluations of ThromboSol, LifeCell's formulation for the extended storage of platelets.

The study will include 20 gynecological cancer patients who are scheduled for chemotherapy at M. D. Anderson and focus on assessing the safety and the clinical efficacy of ThromboSol used to cryopreserve and store rhTPO-stimulated autologous platelets for re-infusion to counter thrombocytopenia during chemotherapy, the company said.

In advance of the chemotherapy, rhTPO will be administered to stimulate production of platelets. This higher-than-normal number of platelets will be harvested and stored frozen in ThromboSol. rhTPO is being developed by Pharmacia & Upjohn Company in the prophylaxis of chemotherapy-induced thrombocytopenia in several cancer indications. The company acquired worldwide marketing rights from Genentech in December 1997.

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Protein Design Labs Inc. (Nasdaq: PDLI) of Fremont, CA, said a phase I trial is underway to evaluate the company's SMART (humanized) 1D10 Antibody in relapsed non-Hodgkin's lymphoma.

The trial is sponsored by NCI under a Clinical Trials Agreement with PDL. Study centers include the University of Iowa Medical School, Cornell Medical School and the Walter Reed Army Institute of Research/Johns Hopkins Medical School.

The SMART 1D10 Antibody binds to an HLA-DR determinant found on many pre-B and B-cell lymphomas. Its target differs from the antibody marketed for the treatment of non-Hodgkin's B-cell lymphoma, which binds to the CD20 antigen, the company said.

The SMART 1D10 Antibody has been shown to kill B-cell tumor lines with equivalent or greater potency than anti-CD20 antibodies, and it has been safely administered to primates in 90-minute infusions. According to the company, the target to which the antibody binds also is present on cancer cells from acute and chronic lymphocytic leukemia patients.

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Valentis Inc. (Nasdaq: VLTS) of Burlingame, CA, announced the initiation of a U.S.-based multi-center phase I/II trial with its interleukin-12 (IL-12) gene therapy for the treatment of squamous cell carcinoma of the head and neck.

The safety phase of the trial was initiated at two sites, the Dana Farber Cancer Institute and the University of Pennsylvania.

Valentis's product uses the IL-12 gene incorporated into the company's polymer-based PINC (Protective, Interactive, Non-Condensing) gene delivery system. The resulting agent is formulated as a stable, single vial, lyophilized product that is easily reconstituted prior to local intratumoral administration.

IL-12 is the third product to enter clinical trials under the collaboration between Valentis and Roche Holdings Ltd. In addition to the IL-12 gene medicine, Valentis is developing IL-2 and Interferon-alpha (IFN-a) under this collaboration. A multi-center U.S. phase II clinical trial of IL-2 began last month.

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Wake Forest University Baptist Medical Center recently became the first medical center to use an innovative treatment system for brain cancer known as the GliaSite Radiation Therapy System.

The Medical Center is one of five NCI-affiliated facilities conducting trials of the investigational device. Developed by **Proxima Therapeutics**, the GliaSite RTS places a high dose of radiation directly into the tissue most likely to contain residual cancer cells following tumor removal.

The device is implanted during the same surgical procedure conducted to remove the tumor and is later filled with a liquid radiation source. Both are removed within several weeks, completing the treatment.

Stephen Tatter, attending neurosurgeon at the Medical Center, is principal investigator of the clinical trials at the Medical Center and national chairman for the study. Studies indicate survival for patients with recurrent malignant brain tumors is approximately three months without therapeutic measures, five months with surgery alone, eight months with surgery and chemotherapy and 15 months with surgery and internal radiation.

Trials evaluating the treatment system are being conducted under the NCI New Approaches to Brain Tumor Therapy program. Other medical centers testing the device are: Johns Hopkins University School of Medicine, Baltimore; Emory University School of Medicine, Atlanta; Henry Ford Hospital, Detroit; and, University of Texas Health Science Center at San Antonio.

Product Approvals & Applications:

FDA Assigns Priority Review To Bexxar For NHL Treatment

Coulter Pharmaceutical Inc. (Nasdaq:CLTR) of South San Francisco, CA, and SmithKline Beecham (NYSE:SBH) said Bexxar (tositumomab, iodine I 131 tositumomab) has been assigned priority review status by FDA, the company said.

That means the license application will be reviewed and action taken by the agency within six months from the June 30 date of submission of a Biologics License Application for the agent, for the treatment of relapsed and refractory, low-grade or transformed low-grade B-cell non-Hodgkin's lymphoma.

Bexxar is a radioimmunotherapy involving an antibody conjugated to I-131 that attaches to a protein found only on the surface of B-cells, the company said.

Coulter and SmithKline Beecham established a partnership to develop and market Bexxar in the U.S. following regulatory approval with the two companies sharing equally in profits. Outside the U.S., excluding Japan, Coulter has granted SB exclusive marketing and distribution rights in return for product royalties.

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Abgenix Inc. (Nasdaq: ABGX) of Fremont, CA, said it has filed an IND to initiate a phase I trial of its proprietary fully human monoclonal antibody, ABX-EGF. The multi-center, multi-dose, dose escalating trial is expected to involve approximately 30 patients with various types of cancer, the company said.

Developed using the company's XenoMouse technology, ABX-EGF targets the receptor for human epidermal growth factor (EGFr) which is overexpressed on many major human tumors types including renal, prostate, lung, and breast. Another

member of the EGFr family, Her-2, is the target for a monoclonal antibody currently being marketed by Genentech, Inc. for treatment of breast cancer.

ABX-EGF binds with high affinity to EGFr and selectively targets these cancer cells by blocking the binding of important tumor growth factors to the receptor, the company said. As reported in Cancer Research (Volume 59, Issue no. 6) in a paper titled, "Eradication of Established Tumors by a Fully Human Monoclonal Antibody to the Epidermal Growth Factor Receptor without Concomitant Chemotherapy," Abgenix demonstrated that ABX-EGF alone, in mouse models, can eradicate established tumors, can block the growth of human tumors, and is potent at comparatively low doses.

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Algos Pharmaceutical Corp. (Nasdaq: ALGO) of Neptune, NJ, said it has received a "not approvable" letter from the FDA for MorphiDex, an NMDA enhanced opioid analgesic. Algos submitted a New Drug Application for MorphiDex in August 1998 for the treatment of moderate to severe cancer pain. MorphiDex is a combination of morphine and the NMDA-receptor antagonist dextromethorphan.

In an Aug. 2 letter to Algos, FDA raised issues specifically related to the adequacy of clinical trials, Algos' preclinical animal toxicology models and a high-dose pharmacokinetic study, the company said.

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American Pharmaceutical Partners of Los Angeles said it has received FDA approval of an Abbreviated New Drug Application for Cisplatin Injection, and was granted a 180-day exclusivity period for the product. APP is in litigation in the federal court in New Jersey with Bristol Myers-Squibb, sponsor of the branded product, Platinol-AQ Injection.

* * *

Diatide Inc. (Nasdaq: DITI) of Londonderry, NH, said it has received approval from the FDA to market NeoTect for the imaging of suspected malignant tumors in the lung. NeoTect is a peptide-based imaging agent intended to help distinguish between benign and malignant lung masses.

NeoTect (kit for the preparation of technetium Tc 99m depreotide injection) is indicated to identify somatostatin receptor-bearing pulmonary masses in patients presenting with pulmonary lesions on computed tomography (CT) and/or chest x-ray who have known malignancy or who are highly suspect for malignancy, the company said.

The methods for determining malignancy are invasive. Biopsy has a complication rate of approximately 14%. Although NeoTect is not considered an alternative to CT or biopsy, Diatide believes that NeoTect can provide important information to help physicians determine whether a lung mass is malignant or benign. NeoTect can deliver this key information to a physician via a noninvasive procedure, yielding significant patient benefit and savings to the healthcare system.

Diatide said the approval triggers a $2 million milestone payment from Nycomed Amersham, a development and marketing partner.

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Eligix, a privately held company based in Medford, MA, said it has initiated a U.S. pilot clinical trial of its BCell-HDM product under an Investigational Device Exemption granted by the FDA. BCell-HDM is being developed for removing malignant lymphoma cells from autologous hematopoietic stem cell grafts in high-dose chemotherapy and transplantation for B-cell lymphomas.

The trial will be conducted in patients with relapsed low or intermediate grade non-Hodgkin's lymphoma. Up to fifteen patients will be enrolled at several sites throughout the U.S.. Several patients have been treated at the Dana-Farber Cancer Institute, Arnold Freedman, of the Dana-Farber is the principal investigator for the trial.

Eligix was incorporated in 1996 by Coulter and by InterWest Partners as an independent, Boston area company and is currently conducting clinical trials of its lead products based on its High-Density Microparticle technology. HDM, in conjunction with the company's portfolio of immune cell-specific and tumor cell-specific monoclonal antibodies, enables the highly efficient separation of specific populations of human blood or bone marrow cells with diverse therapeutic potential, the company said.

HDM is the subject of U.S. Patent No. 5,576,185, issued in 1996, entitled "Method of Positive or Negative Selection of a Population or Subpopulation of a Sample Utilizing Particles and Gravity Sedimentation."

Eligix is developing HDM products for the removal of immune rejection- causing cells from donor-derived stem cell transplants and immune cell infusions, the removal of malignant cells from patient-derived stem cell transplants, and the selection and activation of disease-specific immune cells to enhance a patient's immune response to disease.

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IVAX Corp. (AMEX:IVX) of Miami said the European Commission signed the Decision to grant a Marketing Authorization for Paxene (paclitaxel), in the 15 member-states of the European Union, for the treatment of AIDS-related Kaposi's sarcoma in patients who have failed prior liposomal anthracycline therapy.

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 Ltd., the company's subsidiary in the U.K.

IVAX also has an Abbreviated New Drug Application pending in the U.S. for a generic form of Taxol (paclitaxel). The branded drug, Taxol, is sponsored by Bristol-Myers Squibb.

In May, IVAX presented phase 1 data on Paxoral, an oral paclitaxel system, at the annual meeting of the American Society of Clinical Oncology. Paxoral was developed by Baker Norton Pharmaceuticals, an IVAX subsidiary.

In another development, IVAX said Galena a.s., its subsidiary in the Czech Republic, has begun to market Paxene for the treatment of AIDS-related Kaposi's sarcoma. The product was approved by the Czech Ministry of Health in mid-March but had been awaiting government pricing before launching.

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Orphan Medical (Nasdaq: ORPH) of Minneapolis said that it has received approval from Canada's Therapeutic Products Programme (TPP) to market Busulfex (busulfan) Injection.

The indication provides for use of Busulfex as a conditioning regimen prior to bone marrow or hematopoietic progenitor cell transplantation, when used in combination with other chemotherapeutic agents and/or radiotherapy. Indications under the approval include acute lymphocytic leukemia, acute non-lymphocytic leukemia, acute myeloid leukemia, chronic myeloid leukemia, non-Hodgkin's lymphoma, Hodgkin's disease, multiple myeloma, myelodysplastic syndrome, breast cancer, ovarian cancer and several genetic diseases.

The approval follows a December 1998 submission to the TPP that resulted in an accelerated review for the drug, and represents the second major market approval for Busulfex in 1999. Busulfex was approved in the U.S. on Feb 4, and is the only product approved in the U.S. and Canada for use in pre-transplant conditioning.

Deals & Collaborations:

Abbott, NaPro To Develop Paclitaxel Formulations

Abbott Laboratories (NYSE: ABT) of Abbott Park, IL, and **NaPro BioTherapeutics Inc.** (Nasdaq: NPRO) of Boulder, CO, announced the signing of a long-term collaborative agreement to develop and commercialize one or more formulations of paclitaxel for a variety of cancer indications. The exclusive agreement covers the U.S. and Canada.

"Obtaining access to paclitaxel is a major step in Abbott's plan to expand our presence in the oncology market," said Richard Gonzalez, senior vice president, hospital products at Abbott said.

NaPro will be responsible for supply of the bulk drug and will jointly conduct the clinical trials with Abbott. Abbott will be responsible for the formulation, regulatory filings, marketing and sale of the drug. NaPro will license to Abbott its paclitaxel-related patents including 12 issued U.S. patents and nine pending U.S. patent applications, plus any of its approximately 90 foreign-issued or pending patents which may apply within the U.S. and Canada.

"NaPro has designed a number of novel protocols for the treatment of certain types of cancers and is currently conducting clinical trials in the U.S. and Canada," said Sterling Ainsworth, president and CEO of NaPro. "We have started recruiting sites and investigators for our next phase of pivotal studies." Clinical studies to be pursued by the two companies will investigate several different cancers in a variety of populations."

* * *

Convergence Pharmaceuticals Inc. of Boston, a privately held cancer therapeutics biopharmaceutical company has been acquired by **ILEX Oncology Inc.** (Nasdaq: ILXO) of San Antonio, TX.

Convergence specializes in development of inhibitors of angiogenesis and DNA repair.

ILEX acquired 100% of Convergence in exchange for 1 million shares of ILEX common stock, the companies said. The agreement also provides for an additional earn-out of up to 1 million shares to be issued to Convergence's founders and licensing institutions if development milestones are met.

Convergence's drug pipeline includes six proprietary anti-angiogenic proteins and collagen XVIII derivatives which have shown significant anti-tumor activity in preclinical cancer models, the

companies said. These factors were discovered in the laboratories of two of Convergence's scientific founders, Vikas Sukhatme and Raghu Kalluri, at Beth Israel Deaconess Medical Center and Harvard Medical School. The factors are specific for endothelial cells.

ILEX also acquires NM-3, an orally active small molecule anti-angiogenic drug from the Microbial Chemistry Research Foundation in Tokyo; the commercial manufacturing supply agreement with Mercian, Ltd., also of Tokyo; and licensed technologies involving certain DNA repair targets and lead molecule candidates from ARCH Development.

The merging of the ILEX team with that of Convergence also brings together: Daniel Von Hoff, president of the American Association of Cancer Research and an ILEX founder and board member; Joseph Bailes, president of the American Society of Clinical Oncology and member of the ILEX Board of Directors; Convergence founders, Donald Kufe, Deputy Director of the Dana Farber Cancer Institute and Director of the Oncology Phase I Trials at the Harvard Medical School; and Ralph Weichselbaum, Chairman of Radiation and Cellular Oncology at the University of Chicago.

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Guilford Pharmaceuticals Inc. (Nasdaq: GLFD) of Baltimore said it has received a $2.5 million milestone payment from Rhone-Poulenc Rorer Pharmaceuticals Inc. for regulatory developments relating to Gliadel Wafer in France. Gliadel has been approved for use in France as an adjunct to surgery to prolong survival in patients with recurrent glioblastoma multiforme.

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The Department of Energy's **Lawrence Livermore National Laboratory** has selected **Nomos Corp.** to commercialize Peregrine, a system for targeting tumors during radiation treatment of cancer patients.

The Peregrine dose calculation system accurately predicts radiation doses to tumors during radiation therapy planning. Current dose calculation methods approximate the radiation dose distribution in the patient based on dose distributions in water.

With the Peregrine calculations, doctors can improve treatment design to concentrate radiation doses on tumors, with less damage to surrounding healthy tissue. Peregrine relies on the mathematical technique called Monte Carlo to track radiation. By simulating the trillions of radiation particles that enter the body and tracking their path, Peregrine models the radiation dose absorbed in the patient. Peregrine employs the information from CT scans to tailor radiation dose calculations for each patient, based on the individual's anatomy and disease.

NCI recently introduced a pilot study to compare Peregrine calculations to conventional treatment planning calculations.

* * *

Matritech Inc. (Nasdaq: NMPS) of Newton, MA, said it has submitted to FDA results of a clinical trial documenting its NMP22 Test Kit as an aid in detecting previously undiagnosed bladder cancer.

This expanded use would include testing symptomatic, but previously undiagnosed, patients in the U.S. for bladder cancer. NMP22 is cleared in the U.S. for monitoring for the recurrence of bladder cancer. The results of the submitted clinical study, which included 1,147 subjects at 33 clinical sites in the U.S., demonstrated that the test was 85 percent sensitive in detecting later stage, more life-threatening forms of bladder cancer in previously undiagnosed patients who presented with a risk profile that included smoking and/or hematuria, the company said.

Overall, the test was 70 percent sensitive to all forms of bladder cancer combined.

* * *

Targeted Genetics Corp. (Nasdaq: TGEN) of Seattle said it has signed definitive agreements with **Elan Corp., plc** (NYSE: ELN) to form a new subsidiary of Targeted Genetics with the goal of developing new technologies for the enhanced delivery of therapeutic genes.

Targeted Genetics will own 80.1% of the new company, which is expected to be named Emerald Gene Systems, the companies said. Emerald will be Elan's exclusive effort in the area of gene delivery for a period of at least three years.

Elan made a $5 million investment in Targeted Genetics common stock at a substantial premium to market price. Elan also agreed to buy an additional $5 million of common stock from Targeted Genetics at a premium to market in one year. Elan also bought $12 million of Targeted Genetics convertible exchangeable preferred stock. Proceeds from the sale of the preferred stock will be used by Targeted Genetics to fund its investment in Emerald. Elan has the right to either convert the preferred stock into additional common shares of Targeted Genetics or exchange it for increased ownership in Emerald to 50%.

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