THE CANCER LETTER INTERACTIVE

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

Vol. 28 No. 46
Dec. 13, 2002

As Amgen, Johnson & Johnson Battle Over Anemia Market, Medicare Enters The Fray

Since August, Amgen Inc. has been battling Johnson & Johnson for dominance over the nearly $2 billion U.S. market for drugs that treat cancer-related anemia.

Amgen's marketing campaign was built around price incentives and greater convenience for patients. Marketing materials obtained by **The Cancer Letter** show that Amgen claimed that its recently approved agent Aranesp (darbepoetin alfa) produced greater net revenues for hospitals and physicians' practices than J&J's Procrit (epoetin alfa).

Though the two companies generated enough data to win FDA

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In Brief:

Foundation Gives $1 Million To UPCI For Endowed Cancer Genetics Chair

UNIVERSITY OF PITTSBURGH CANCER INSTITUTE raised $2.1 million at a Dec. 3 gala. **David Shapira**, chairman and CEO of the Giant Eagle Foundation, announced a $1 million gift to UPCI that will be used to establish a Giant Eagle Endowed Chair of Cancer Genetics. The chair will enable UPCI to recruit new talent and to expand the body of knowledge about genetic susceptibility of cancer. More than 650 people attended the event, including actress and breast cancer survivor **Ann Jillian**. . . . **C-SPAN's** "Washington Journal" program on Nov. 26 included interviews with NIH Director **Elias Zerhouni** and NCI Director **Andrew von Eschenbach**. Zerhouni discussed the mission of NIH, review of the NIH organizational structure, health disparities, and the types of clinical trials conducted at the NIH Clinical Center. Von Eschenbach addressed several topics, including plans to expand basic research and prevention research, reasons for improvements in cancer survival rates, and differences in funding for breast and prostate cancer. The interviews are available in video at www.c-span.org/journal/. . . . **FDA COMMISSIONER MARK MCCLELLAN**, speaking at a conference in Houston last week, said his agenda for the agency includes four priorities: to ensure a strong, science-based FDA; to protect the public's health against a potential terrorist attack; to help consumers get reliable information about FDA-regulated products; and to reduce preventable adverse health events from FDA-regulated products. Text of his remarks is available at www.fda.gov/oc/speeches/2002/healthservice.html. . . . **CLARIFICATION:** In last week's issue of **The Cancer Letter**, it was

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CMS Asks NCI For Trial Of Aranesp vs. Procrit

(Continued from page 1)

approval, neither has optimized the dosing schedules or generated comparative data on the two cancer-related anemia agents, which together constitute the single largest segment of the oncology market (**The Cancer Letter**, Aug. 2).

Information provided by J&J recently convinced Centers for Medicare and Medicaid Services that Amgen's Aranesp was so similar to Procrit that it should be reimbursed at the same rate for doses associated with similar clinical results.

CMS said it will cut Aranesp reimbursement in half for Medicare beneficiaries receiving the agent as hospital outpatients through Medicare Part B. In a move that appears to be unprecedented, CMS asked NCI to compare the two agents head-to-head.

Amgen pledged to cooperate with the NCI trial, but is fighting the Medicare rule. The company said hospital outpatients on Medicare account for 10 percent of the market for Aranesp. However, a lot more is at stake for the company. Reimbursement decisions made in Medicare Part B can spill over into Part A, which covers physicians' offices, where the majority of patients receive cancer care. Private insurers, too, would be likely to follow the government's lead.

If all goes according to the CMS plan, on Jan.1, 2003, Medicare reimbursement for hospital administration of Aranesp to outpatients will be cut roughly in half. Consider the impact of the change on the price of Aranesp given to a Medicare patient weighing 70 kg:

—At the dose of 1.5 mcg/kg, which is marketed as the starting point for patients receiving Aranesp, physicians now bill $497.66. On Jan. 1, the bill will have to drop to $248.85. The largest share of these bills—80 percent—is paid by Medicare. The rest is picked up by the patient.

—At the FDA-approved dose of 2.25 mcg/kg, physicians bill $746.63. Next month, this will drop to $373.28.

—The maximum studied dose of 4.5 mcg/kg costs $1,493.25. After the change, this will drop to $746.55.

To prevent this cut, which is calculated to equate the reimbursement for Procrit and Aranesp, Amgen sued CMS in the U.S. District Court for the District of Columbia, seeking an injunction. "We will take every legislative, legal, and commercial action available to us," said Barbara Bronson Gray, Amgen associate director, corporate communications. "That's what's happening now."

A court decision is expected in late December.

CMS: Agents "Functionally Equivalent"

Arguing that Procrit and Aranesp are "functionally equivalent," CMS said the Amgen agent would no longer be reimbursed through "pass-through" payments, which are used to pay for drugs and biologics during their first two to three years on the market.

"These two biologicals should be paid at the same rate," CMS said in its "final rule," published in Federal Register. "The products are almost identical; nevertheless there is a great disparity in their costs. In this situation, we believe it is appropriate for us to rely on our authority… to make an adjustment we determine 'necessary to ensure equitable payments.'

"We do not believe it would be equitable or an efficient use of Medicare funds to pay for these two functionally equivalent products at greatly different rates," the document states.

Though CMS has derived an estimate of a conversion scale for the two agents, it did so with the understanding that Procrit and Aranesp must be compared in clinical trials.

The two agents have different molecular structures and are measured in different units.

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

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Subscription $305 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd

Aranesp has two more carbohydrate chains than Procrit and is measured in micrograms per kilogram (mcg/kg), while Procrit is measured in Units per kilogram of a patient's weight.

According to Amgen, the dose of 40,000 Units of Procrit once a week is equivalent to 200 mcg of Aranesp every two weeks for a 70-kg patient. There is no formula for converting agents dosed in Units to doses measured by weight.

To find the significance of these differences, CMS turned to NCI. "We think that improved information from clinical trials involving 'head-to-head' comparisons of these two products could help us insure our policy is correct and if necessary update this policy in the future," CMS wrote in the final rule. "In this vein, the NCI has been directed to work with CMS to quickly develop and sponsor a trial or trials to evaluate the appropriate conversion ratio between these products for the purpose of Medicare pricing."

NCI Trial To Address Broader Questions

Usually, scientific questions for NCI-sponsored trials emerge in academia, in clinical practice, or at the Institute. The question for this trial, by contrast, emerged at CMS, and was conveyed through HHS, sources said.

Yet, academics and NCI officials said the question is both scientifically compelling and likely to influence medical practice.

"This is important to patients and to clinicians who see them week after week," said Richard Kaplan, chief of the Clinical Investigations Branch in the NCI Cancer Therapy Evaluation Program. "Patients want to know that they are getting the most help available to them to get through chemotherapy or cancer-related anemia as effectively as they can, to diminish side effects of therapy.

"And, obviously, this is a very expensive class of agents, and everybody would like to feel that we are using the resources the best way we can," Kaplan said.

The question posed by CMS is seemingly narrow: determine the conversion ratio between the two agents.

In the absence of conclusive justification for optimal dosage of either of the two agents, the Institute and academic investigators found themselves confronting a series of scientific questions.

"There are lots of data that various regimens are efficacious for half the patients or so," Kaplan said. "What we don't know includes whether one or another schedule can increase the proportion of patients who respond, whether one or another schedule can speed up the response for patients who are going to respond, whether there are ways to effectively predict which patients will respond, and which patients will need a change in dosage in order to respond.

"We don't know exactly the shape of the dose-response curve for either of these two preparations, and if we knew the shape of it better, we might be able to better develop a strategy which is both economical and likely to be effective in most patients," Kaplan said.

Charles Loprinzi, chairman of medical oncology and principal investigator of the Community Clinical Oncology Program research base of the North Central Cancer Treatment Group, said the trial would seek to answer four questions:

"The questions are: (1) Which is the better of the two agents, if either? (2) Which is the most appropriate schedule of the agents? (3) What is the appropriate dose to use; is it small dose, intermediate dose, or large dose? (4) If they are all equal, then what's the best treatment to give, and what's the most economical way to give that treatment?"

Investigators Will Design the Trial

NCI's Kaplan said clinical investigators are taking the lead in designing a trial, and the structure is likely to emerge by the end of the month, he said.

Cancer-related anemia is an elusive subject, and the questions Kaplan and investigators are wrestling with are anything but simple. Anemia is observed in many clinical settings, from adjuvant to end-stage. In some cases, it's caused by treatment; in others, it's a byproduct of the disease.

How would one define the populations for the study? Should it be a distinct trial available to all patients willing to take part, or should it be some composite reflecting the mix of populations enrolled in a variety of NCI-sponsored trials?

"Do you conduct a specific, tightly controlled trial, which will take you longer to do, versus making

The Cancer Letter Takes Winter Publication Break

This issue, Vol. 28 No. 46, Dec. 13, is the final issue of **The Cancer Letter** for 2002.

The next issue, Vol. 29, No. 1, is scheduled for publication Jan. 3, 2003.

it more broader, general, to affect the real-life practice? That's the question at hand," said Loprinzi, who is involved in designing the trial.

"If you pick a single disease and a single chemotherapy regimen, some people might say, that's the ideal thing: everybody is getting exactly the same thing, so it's all well-controlled," Loprinzi said. "But, what happens if you picked the wrong disease and the wrong chemotherapy?"

Piggybacking the trial to some mixture of treatment trials has advantages and disadvantages, too, Loprinzi said.

"A pro might be that you might have more controlled data," he said. "A con is that it may be difficult to administer that sort of a process and to interpret the data. The other option is a larger, simpler trial where you just allow random chance to define the variables that are there."

The question of the optimal dose is on the table, too. "Do you use the FDA-approved dose? Do you use the marketed dose? Or do you use the dose mostly used in clinical practice?" Loprinzi said.

"These are factors that need to be decided upon."

Though Amgen is fighting the CMS rule, it supports the NCI study the agency requested. "We think it needs to be done," said Amgen spokesman Gray. "We will do whatever they need us to do. If they need drug, I am sure we will make it available."

J&J, too, is cooperating. "We support and respect CMS's efforts to ensure that their policy is accurate and fair," said Carol Goodrich, a J&J spokesman. "We would hope that these clinical trials accomplish that objective."

The CMS rule states that NCI would be expected to complete the trial within about a year, by the time the 2004 Medicare payment schedule is developed.

"Get Rolling" With Aranesp

After Aranesp was approved for the treatment of cancer-related anemia last July, Amgen launched an aggressive campaign to eclipse the J&J control of the market.

The message to physicians was clear: switch from Procrit to Aranesp, and you will make more money.

According to marketing materials, a 25 mcg vial of Aranesp generated net revenues of $38.61, which happens to be $1.51 more than the equivalent vial of Procrit. Greater amounts generated bigger revenues: a 60 mcg vial brought in $70.52, beating Procrit by $12.32.

Profits, too, were affected. Under Amgen's "Get Rolling" program for Aranesp, physicians were offered 20 percent discounts on 25 mcg and 60 mcg vials of Aranesp, marketing materials said. Since the acquisition price is lower than the AWP minus 5 percent rate split by Medicare and the patients, the Get Rolling rebate amounted to an additional 20 percent markup.

Critics, particularly J&J officials, maintained that the Aranesp starting dose marketed by Amgen was unrealistic.

The marketed dose—1.5 mcg/kg—was lower than the 2.25 mcg/kg dose approved by FDA. Yet, at the lower dose, the price of Aranesp was a little lower than the price of an equivalent amount of Procrit.

Outmaneuvering J&J, Amgen made a supply agreement with Houston-based U.S. Oncology Inc. The network of practices that treats 15 percent of all newly diagnosed cancer patients in the U.S. designated Aranesp as the preferred treatment for anemia.

On July 31, Texas Oncology P.A., the largest practice managed by U.S. Oncology, notified its 197 physicians that henceforth they would have to obtain approval from regional directors in order to use Procrit and two other "non-formulary" drugs, Zometa and Zofran. (TOPA's formulary includes Pamidronate and Anzemet.)

"If the use is not approved, the physician ordering the non-formulary drug will be charged the difference between the margins of formulary and non-formulary drugs," TOPA president R. Steven Paulson said in the memo.

"There will be a three-month trial period before the financial penalties take effect, during which physicians will be notified, but not charged, the amount of penalty they would have incurred had the plan been effective. After the three-month trial, which will end Sept. 30, the penalties will be assessed and recovered by offset against the monthly bonus," the memo said.

"We know all of you are busy, and have concerns about adding another hassle factor to your already busy day. However, data indicates that limiting use of the non-formulary drugs could save TOPA in excess of $1 million per year."

In an interview, Paulson said the TOPA policy inserts an extra step designed to make physicians stop for a moment and think before they prescribe Procrit.

"The idea is to instruct and inform, not to

punish," Paulson said. "That one little step puts in there, 'Okay, I need to think about this.' It's a means of stimulating a physician to actually think about what he is doing, instead of reacting to the last pharmaceutical representative who was in his office."

The decision to place Aranesp in the formulary was made by the U.S. Oncology Pharmacy and Therapeutics Committee and the TOPA board, which reviewed the data and decided that "the drug is cheaper to the patients, it's cheaper to the payer, it's more convenient to the patients, because they can come in every two weeks instead of every week to get the drug, and, financially, it's probably more advantageous to us," Paulson said.

TOPA has not used financial penalties in the past, Paulson said.

"If they don't communicate at all, if they say, 'I am going to use it regardless of what anybody says,' then there probably are some folks who have been dinged a trivial amount of money," Paulson said.

"But the reality is that all you have to do is pick up the phone or send me a request that says I want to use Procrit," he said. "You don't even have to give me a reason, and 100 percent of all requests for Procrit have been approved. It's a matter of physician's choice, and if a physician says, 'I want to use Procrit,' it's fine. It doesn't even have to be a physician. A nurse can call. A nurse can fax in a request. It's 100 percent approved. I have never turned anybody down, and the two other medical directors who get occasional telephone calls on that have not turned anybody down."

About two out of three patients who receive anemia treatment at TOPA get Aranesp, and the practice is tracking the data on the two agents, Paulson said. "Our group is large enough that we can collect that data," he said. "One of the things we can follow is Aranesp failures and Procrit failures, those are fairly easy to track, and there doesn't seem to be a whole lot of difference."

Paulson said he hopes to have the raw data collected by April 1. "When you have 140 to 150 medical oncologists, and you have access to information, we can tell pretty quickly whether we are on the right page, or whether we need to turn the page," Paulson said.

J&J Sought CMS Review

Originally, CMS did not plan to cut reimbursement for Aranesp. An earlier version of the regulation, published in the Federal Register Aug. 9, extended the pass-through status to the Amgen agent.

However, on Oct. 1, J&J submitted its comments on the regulation, arguing that reimbursement of Aranesp at a higher rate than Procrit would create "perverse incentives" for hospitals to switch their patients to the more expensive drug.

"The cost of [Aranesp] to the Medicare program is 80 percent higher than the cost of [Procrit]," Gary Reedy, president of Ortho Biotech Products L.P., said in a 15-page letter to CMS.

The CMS final rule, published in the Federal Register Nov. 1, credits J&J with bringing the issue to the agency's attention.

"A drug company raised concerns about the relationship of [Procrit] and [Aranesp], two competing biologicals used for treatment of anemia," the agency said. "The commenter urged that CMS determine that the two products are substitutes with the same clinical effects and argued that the two should be paid, subject to an appropriate conversion ratio, at the same rate."

According to the CMS final rule, the agency met with the two companies, and hired an outside expert to review the data. The text of the final rule is posted on the U.S. Government Printing Office Web site: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=2002_register&docid=page+66717-66766

In a suit filed in the U.S. District Court for the District of Columbia, Amgen counters that the agency's rule exceeds its statutory authority.

The action was "in direct conflict with the pass-through statute, which authorizes reductions in pass-through payments, but only where necessary to keep total pass-through expenditures within a statutory cap," the company's complaint states. "Even then, the statute specifically provides that all such reductions will spread among all pass-through products pro rata. The statute contains no authorization for CMS to pick and choose among pass-through products, imposing cuts on one and leaving the rest."

According to the suit, "CMS attempted to justify doing so here by devising a new 'functionally equivalent' scheme for comparing new drugs with older ones." The words "functional equivalence" have not been previously used in CMS regulations, the complaint states.

"CMS' action in this regard violates the Administrative Procedure Act, because it (1) exceeds CMS' statutory authority; (2) is arbitrary and

capricious because the rule singles out one product for special treatment based on unreliable and inadequate data not intended by Congress to be used for these purposes; and (3) violates the APA and due process, because CMS failed to provide notice of its intended action," the complaint states.

Amgen and J&J have a long history of discord, much of it revolving around erythropoietin.

Procrit was developed by Amgen and licensed to J&J for the U.S. cancer market in 1985. The company's cancer unit, Ortho Biotech, created the market through direct-to-consumer advertising, but did not develop the agent's clinical potential.

Amgen made several attempts to break out of the agreement, under which it continues to manufacture Procrit. After Amgen altered the molecular structure of erythropoietin to increase its half-life and require less frequent administration, J&J tried to block the introduction of the new agent.

J&J argued unsuccessfully that the new version of the agent, Aranesp, is not sufficiently different from Procrit to be regarded as a new drug. While this argument has failed in the courts, it appears to have persuaded CMS.

NCI Policy:

NCI Equivocates On Statement About Abortion, Breast Cancer

Under pressure from abortion opponents, NCI has weakened its assessment of published research examining whether having an abortion changes a woman's risk of developing breast cancer.

A statement posted on the NCI Web site Nov. 25 draws no conclusion about breast cancer risk in women who have had abortions, and characterizes the available data as "inconsistent."

More than 30 published studies since 1957 have examined the "possible relationship between abortion and breast cancer," the statement said. "Some studies have reported statistically significant evidence of an increased risk of breast cancer in women who have had abortions, while others have merely suggested an increased risk. Other studies have found no increase in risk among women who had an interrupted pregnancy."

That ambiguous statement contrasts sharply with a "fact sheet" posted on the Institute's Web site last March, which concluded that "the current body of scientific evidence suggests that women who have had either induced or spontaneous abortions have the same risk as other women for developing breast cancer."

The earlier statement discussed the largest and most reliable cohort study, reported by Danish researchers in the New England Journal of Medicine in 1997. That study used health information from registries for 1.5 million Danish women, was not subject to recall bias, and found that induced abortion had no overall effect on the risk of breast cancer.

The new NCI statement provides no information about this study.

It was not a change in scientific consensus that caused NCI to alter its statement. The Institute removed the fact sheet from its Web site last June after receiving a letter from Rep. Chris Smith (R-NJ) and 27 other members of Congress known to oppose abortion. The letter demanded that NCI take down the fact sheet and claimed that most of the published studies show abortion increases the risk of breast cancer—an assertion that NCI disputed in a response to a Congressional inquiry in 1999 (**The Cancer Letter**, Vol. 28 No. 28, July 12, 2002).

The new statement is intended as an "interim statement" until the final report of an NCI workshop on early reproductive events and breast cancer, to be held next year, NCI spokesman Dorrie Hightower said.

"Further scientific research needs to be done to determine and to investigate the relationship of breast cancer to hormone changes that occur with pregnancy," the new NCI statement said.

The NCI statement is posted at www.cancer.gov/cancer_information/doc.aspx?viewid=8cf78b34-fc6a-4fc7-9a63-6b16590af277.

In contrast, the American Cancer Society concludes that, "Research studies have not found a cause-and-effect relationship between breast cancer and abortion."

An article posted on the society's Web site notes that most of the early studies of abortion and breast cancer used a case-control study design, which is prone to recall bias. "Studies have shown that healthy women are les likely to report their histories of induced abortions," the article said. "In contrast, women with breast cancer are more likely to accurately report their reproductive histories because they are literally searching their memories for anything that may have contributed to their disease."

Also, induced abortions were illegal in the U.S. until 1973. Women in the earlier studies may not have

wanted researchers to know they had an illegal abortion, the society said.

"It is likely that the small increases in breast cancer risk observed in many of these studies were not authentic findings because of recall bias," the society said.

The ACS article said the Danish study's size and methods "provides substantial evidence that induced abortion does not affect a woman's risk of developing breast cancer."

The society's article said "false alarms" about breast cancer risk do not serve the public:

"The issue of abortion generates passionate personal and political viewpoints, regardless of any possible disease connection. Breast cancer is the second most common cancer in women, and it can be a life-threatening disease that most women fear. Still, the public is not well-served by false alarms, even with both the exposure and the disease are of great importance and interest to us all. At the present time, the scientific evidence does not support a causal association between induced abortion and breast cancer."

The ACS statement is available at: www.cancer.org/docroot/CRI/content/CRI_2_6x_Can_Having_an_Abortion_Cause_or_Contribute_to_Breast_Cancer.asp

Funding Opportunities:
Program Announcements

PA-03-041: High-Impact Pilot Studies in Cancer Biology

NCI invites R21 exploratory/developmental grant applications for high-impact pilot studies in basic cancer biology. Examples of appropriate research areas include, but are not restricted to, how variations in genes combine with the cellular environment to cause cancer; development of new experimental models that parallel human cancer-related pathways and processes; and exploration of new molecular pathways in cancer biology, particularly those that could lead to novel targets. PA is available at http://grants1.nih.gov/grants/guide/pa-files/PA-03-041.html.

Inquiries: Barbara Spalholz, Division of Cancer Biology, NCI, EPN 5034, Bethesda, MD 20892-7396; phone 301-496-7028; fax 301-402-1037; e-mail bs62d@nih.gov.

PAR-03-035: Human Brain Project: Phase I—Feasibility; Phase II-Refinements, Maintenance and Integration

Letter of Intent Receipt Dates: One month prior to receipt date

Application Receipt Dates: Jan. 21, May 21, Sept. 22, 2003; Jan. 21, May 21, Sept. 22, 2004; Jan. 21, May 20, Sept. 22, 2005

The initiative supports research that will lead to the development of web based databases, analytical tools, and knowledge management systems to promote sharing of data for all domains of neuroscience research. The PA is available at http://grants1.nih.gov/grants/guide/pa-files/PAR-03-035.html.

Inquiries: Guoying Liu, DIP/DCTD, NCI, 6130 Executive Blvd. Room 6062, MSC 7412, Bethesda, MD 20892-7412, phone 301-594-5220; fax 301-480-3507; e-mail liug@mail.nih.gov.

In Brief:
Brennan, Demetri Co-Chair Sarcoma Foundation Board

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incorrectly reported that Anna Barker will work part-time at NCI as deputy director for strategic scientific initiatives. She began working full-time after Dec. 1. She previously had worked part-time as a consultant prior to her appointment to the new position. . . . **SARCOMA FOUNDATION OF AMERICA** has appointed **Murray Brennan**, of Memorial Sloan-Kettering Cancer Center, and **George Demetri**, from Harvard Medical School, as co-chairmen of its medical advisory board. The foundation is extending the deadline for research grant proposals to Jan. 31. Submissions should involve research that could lead to the development of novel agents against sarcoma. Grants up to $25,000 are available. Further information available at www.curesarcoma.org. . . . **SHIRLEY MALCOM** was awarded the Public Welfare Medal by the National Academy of Sciences for her 30 years working at the grass-roots level and internationally to improve science and technology education and participation by students of diverse backgrounds. "Dr. Malcom has served science with extraordinary scope, originality, and achievement," said **R. Stephen Berry**, home secretary of the NAS and chairman of the selection committee. Malcom is head of the Directorate for Education and Human Resources of the American Association for the Advancement of Science. . . . **ROSWELL PARK** Cancer Institute announced the following appointments: **Christine Ambrosone** was named chairman of epidemiology, Department of Cancer Prevention and Population Sciences. She was associate professor and director, Cancer Epidemiology Program, Derald H. Ruttenberg Cancer Center, Mount Sinai School of Medicine. **Donald Trump**, senior vice president of clinical research and chairman, Department of Medicine, was appointed

editor-in-chief of the journal Oncology. He succeeds the late **Paul Carbone.** In another development, RPCI opened the renovated **Edwin A. Mirand Library**, an $850,000 project. . . . **ANAND JILLELLA** joined Fox Chase Cancer Center as associate director of the Fox Chase-Temple Bone-Marrow Transplant Program and associate professor of medicine at Temple University School of Medicine. Jillella directed the Stem-Cell Transplant Program at the Medical College of Georgia in Augusta. **Kenneth Mangan** directs the Fox Chase-Temple program. Also at Fox Chase, **Sven-Erik Behrens** joined the division of basic science. His research will focus on the hepatitis C virus and cancer. . . . **ALBERT DE LA CHAPELLE** received the 2002 William Allan Award from the American Society of Human Genetics at the society's annual meeting in Baltimore. De la Chapelle directs the Human Cancer Genetics Program, Ohio State University Comprehensive Cancer Center, and is Charlotte and Leonard Immke Chair of Cancer Genetics. . . . **SISSY JHIANG**, associate professor of physiology and cell biology and internal medicine at Ohio State, and member of the OSUCCC Molecular Biology and Cancer Genetics Program, won the Van Meter Award from the American Thyroid Association. The annual award honors young scientists under the age of 45. . . . **HARVEY BICHKOFF,** CEO of California Cancer Care, an oncology group in the San Francisco Bay Area, was elected president of the Administrators in Oncology/Hematology Assembly, a special-interest group of the Medical Group Management Association. The AOHA represents about 600 group practice administrators. . . . **MEMORIAL SLOAN KETTERING** Cancer Center has begun a Web site with information about herbs, botanicals, and vitamins for oncologists and healthcare professionals. It includes a clinical summary for each agent and details about constituents, adverse effects, interactions, and potential benefits or problems. Evaluations of alternative or unproven cancer therapies are also provided. The site is available at www.mskcc.org/aboutherbs. . . . **FDA** posted a Web site with information about the agency's ethics program, which is designed to help ensure that decisions made by agency employees are not tainted by any question or appearance of conflict of interest. The site provides guidance about issues such as gifts and awards, financial interests, outside employment, and political activities: www.fda.gov/opacom/ethics/.

THE CANCER LETTER

Vol. 17 No. 11
December 2002

Business & Regulatory Report

Deals & Collaborations:

Pfizer, Pharmacia Shareholders Approve Pfizer's $55.5B Purchase Of Pharmacia

Shareholders of both Pfizer Inc., of New York, and Pharmacia Corp., of Peapack, N.J., voted earlier this month to approve Pfizer's proposed $55.5 billion purchase of Pharmacia.

Pfizer shareholders agreed to let the company issue more stock, most of which will be used to buy Pharmacia. Under an agreement the companies reached last July, Pharmacia shareholders will receive 1.4 Pfizer shares for each Pharmacia share. Pfizer expects to issue 1.8 billion

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Product Approvals & Applications:

FDA Approves Taxotere As First-Line Therapy For Advanced Lung Cancer

FDA approved Taxotere (docetaxel, **Aventis**) as first-line therapy in patients with unresectable locally advanced or metastatic non-small cell lung cancer in combination with cisplatin, who have not received prior chemotherapy.

With this FDA approval, Taxotere is the only agent indicated both for patients with newly diagnosed NSCLC, in combination with cisplatin, and for those with previously treated advanced NSCLC, as a single agent.

The approval was based on a clinical trial with 1,218 patients, comparing the effect of Taxotere plus cisplatin or Taxotere plus carboplatin to a standard regimen of vinorelbine plus cisplatin. Patients in the Taxotere plus cisplatin group had a median survival time of 10.9 months vs. 10.0 months for patients treated with vinorelbine plus cisplatin. The overall response rates were 31.6 percent for Taxotere plus cisplatin vs. 24.4 percent for vinorelbine plus cisplatin.

Additional study analysis indicated that the benefits seen in the study were maintained in patients who were 65 years of age and older. According to data from NCI, 68 percent of all lung cancer patients are 65 years of age and older.

Taxotere is approved in the U.S. to treat locally advanced or metastatic breast cancer after failure of prior chemotherapy, and locally advanced or metastatic NSCLC after failure of prior platinum-based chemotherapy.

Last September, the Committee for Proprietary Medicinal Products issued a positive recommendation for Taxotere in Europe for the first-line treatment of advanced NSCLC in combination with cisplatin.

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Pfizer Purchase Expected By End Of First Quarter

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shares to complete the deal. Those shares are worth about $55.5 billion at recent prices.

At the Pharmacia shareholders meeting Dec. 9, about 71 percent of outstanding shares, and 99 percent of the total votes cast, were cast in favor of the transaction. The positive vote by Pharmacia shareholders follows a meeting of Pfizer shareholders on Dec. 6 at which more than 96 percent of the votes were cast in favor of the transaction.

The purchase is expected to be completed by the end of the first quarter next year. U.S. and European regulators are still reviewing the deal.

"Pfizer and Pharmacia represent a compelling strategic combination," said Hank McKinnell, Pfizer chairman and CEO.

Pharmacia makes the cancer drug Camptosar as well as Rogaine hair products and the Nicorette smoking cessation line. Pfizer sells the cholesterol-lowering agent Lipitor and erectile dysfunction drug Viagra.

Pharmacia is a marketing partner for Pfizer's Celebrex arthritis drug franchise.

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Allergan (NYSE:AGN) of Irvine, Calif., has entered into a research collaboration and license agreement for the right to develop and commercialize PEP005 for the topical treatment for non-melanoma skin cancer and actinic keratosis from **Peplin Biotech Ltd** (ASX:PEP) of Brisbane, Australia.

Under the agreement, Allergan obtains an exclusive license to develop and commercialize PEP005 for the topical and intralesional treatment of skin and eye conditions in North and South America, the company said. Peplin may receive up to $23 million in milestone and other payments and a market-rate royalty on net sales.

"We have been impressed with the pre-clinical study results on Peplin's lead compound PEP005 and its potential in the large, growing and under-served market for treating non-melanoma skin cancer," said David Pyott, chairman of the board, president and CEO of Allergan.

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Beyond Genomics Inc. of Waltham, Mass, said it has entered into an evaluation agreement with **GlaxoSmithKline** to apply the Beyond Genomics systems biology approach to study disease and drug response.

The goal is to discover biosystem markers, and to better understand proteins and metabolites that play roles in mediating disease states and response to drugs, the company said.

Financial and additional deal terms were not disclosed, the company said.

The BG technologies include a number of high-throughput, next generation genomic, proteomic and metabolomic platforms, the company said. Biosystem markers identified by BG are further characterized to determine their roles in disease and drug response. The company said it also employs proprietary pattern recognition, clustering, and data mining software to integrate and analyze data into the mechanisms of disease and drug response.

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CADx Systems Inc. of Beavercreek, Ohio, said it has signed a development and distribution agreement with **GE Medical Systems**, a unit of General Electric Co. (NYSE:GE) for the CAD breast screening technology.

Under the terms of the agreement, GE Medical Systems will integrate the CADx Systems Second Look computer aided detection software for use with the GE Senographe 2000D full-field digital mammography system, the company said.

"Our agreement with CADx will allow Senographe 2000D users around the world with access to another advanced technology for early

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

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

Business & Regulatory Report

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

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

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

Business & Regulatory Report, a supplement to The Cancer Letter, is available separately for $185 per year. ISSN 1053-9611.

breast cancer detection," said Dow Wilson, general manager of surgery, X-ray and interventional imaging, GE Medical Systems.

Studies have shown that up to 23 percent of breast cancers could have been discovered on average 15 months earlier with the use of Second Look, the company said.

The GE Senographe 2000D is based on proprietary technology developed by GE to produce digital X-ray images without film and is designed to generate digital mammographic images that can be used for the screening and diagnosis of breast cancer, the company said. The system utilizes breakthrough software technology to highlight areas of concern on a Mammagraph report, calling attention to subtle changes in tissue that may indicate the presence of cancer.

Integration of the GE Senographe 2000D and the CADx Second Look CAD software will require FDA clearance for clinical use in the U.S., the company said. The companies said they are preparing FDA pre-market approval supplements.

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ChemBridge Research Labs. LLC, of San Diego, and the **Genomics Institute of the Novartis Research Foundation** said they have signed a three-year targeted library agreement.

Under the agreement, CRL will provide to GNF and GNF affiliates, including Novartis AG, non-exclusive access to its GPCR-targeted library of small molecules based on non-peptide chemotypes, the companies said.

Also, under the agreement, GNF will provide screening data to CRL relating to the provided compounds, and GNF has the ability to take advantage of additional hit-to-lead follow-up services from CRL, the companies said.

Other terms were not disclosed, the companies said.

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CytoGenix Inc. (OTCBB:CYGX) of Houston said it has formed a scientific collaboration with Madeleine Duvic, professor of internal medicine and dermatology, Division of Internal Medicine and deputy chairman of dermatology, **The University of Texas M. D. Anderson Cancer Center** in Houston, to investigate, test, and evaluate a gene related to melanoma.

The CytoGenix scientific team will be using its proprietary ssDNA Expression System to construct and deliver target-specific gene knockout sequences to melanoma cancer cells, the company said.

Duvic is associate medical director of the Melanoma and Skin Center at M.D. Anderson Cancer Center.

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Genomics Collaborative Inc. of Cambridge, Mass., has signed an agreement with the **Genome Institute of Singapore** and the **Agency for Science, Technology & Research** to build a DNA and tissue sample repository for the Government of Singapore.

The Singapore Tissue Network will be linked to a clinical phenotypic database from the National Disease Registry Office, Ministry of Health, Singapore, the company said. Under the guidance by the Ministry of Health in Singapore for policies, the network will provide the infra-structure for the nationwide collection, processing, quality control, archiving and distribution of high quality, annotated tissue and DNA samples.

Specific terms of the agreement were not disclosed, but the licensing and consulting agreement will last for three years with an option to renew the software licensing, the company said.

"We believe that Singapore is well positioned for the establishment of a strategic national repository given the well organized health care system and advanced technologies and medical informatics," said Edison Liu, director of the Genome Institute of Singapore.

GCI will provide services including advising on staff and physician recruitment, sample collection, tracking, processing, storage, and retrieval, the company said. In addition, GCI will provide advice on data collection, database generation, as well as software systems management, integration and operation.

"A national tissue repository is a new concept that is in line with the global trends of data centralization and the pooling of critical resources for specific applications," said Philip Yeo, chairman of the Agency for Science Technology and Research. "One example of this emerging trend of repository is the half million subject UK BioBank Project to investigate effects of genetic and environmental factors on human diseases. Another example is the collection of high-quality cancer tissues for a clinical databank in the UK. The discoveries from these kinds of population research will lead to applications to prevent and cure illnesses, which can greatly reduce health care costs."

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Genesis Bioventures Inc. (AMEX:GBI) of New York, N.Y., said it has signed a binding letter of intent for a business combination with **Innathera Inc.**

The transaction is subject to the execution of a definitive agreement and related conditions, the company said. The parties are seeking to complete a definitive agreement on or before the end of the year.

"The merger would combine the diagnostic strengths of Genesis Bioventures's technologies with the therapeutic focus of Innathera's technologies," said Greg McCartney, chairman and CEO of GBI. "The addition of Innathera's compounds in conjunction with the use of our diagnostic tools creates a compelling opportunity for GBI in the fight against cancer. The Innathera team brings years of experience in the biotechnology arena, in both finance and commercial development of products."

The proposed combination is subject to due diligence, execution, and delivery of definitive documentation, approval by boards of directors and shareholders of the companies, and completion of arrangements for a $15 million equity financing to allow the combined companies a significant resource base with which to continue to develop and commercialize the technologies, and customary closing conditions, the company said.

The merged companies will focus on the development and the global commercialization of the Mammastatin Serum Assay, breast cancer risk assessment tool, the associated diagnostic assays for prostate and ovarian cancer, as well as the development of Innathera's two anticancer compounds, the company said. Those compounds are Inath 011, which is a monoclonal antibody that has been shown to reduce the proliferation of breast and prostate cells, and Inath 016, an angiogenesis agent that has shown efficacy in colorectal and liver cancer, the company said.

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ILEX Oncology Inc., of San Antonio, Tex., (Nasdaq:ILXO) has signed the first of several expected sublicensing agreements intended to rapidly commercialize Campath-related diagnostic testing worldwide.

The company has signed a letter of intent to sublicense to **Ventana Medical Systems** (Nasdaq:VMSI) exclusive worldwide diagnostic rights to develop and commercialize an immuno-histochemistry test to detect the presence of the CD52 antigen in lymph nodes and potentially in certain solid tumors.

"The agreement with Ventana is an important first step toward making commercial CD52 diagnostic testing available to physicians," said ILEX President and CEO Jeffrey Buchalter. "Ventana systems are present in about 80 percent of the major cancer centers in the U.S. A standardized test will accelerate the routine screening of the CD52 antigen, which, according to recent findings, appears to be associated with several types of cancer, including lymphomas, in addition to B-cell chronic lymphocytic leukemia (B-CLL). It will also serve as a valuable tool enabling ILEX clinicians to pinpoint cancers in which Campath may play a key therapeutic role."

Campath (alemtuzumab) is approved in the U.S. for the treatment of patients with B-CLL who have been treated with alkylating agents and failed fludarabine therapy. The drug works by targeting the CD52 antigen, resulting in the removal of malignant lymphocytes from the blood, lymph nodes, bone marrow and other affected organs.

To broaden the scope of testing for CD52, ILEX expects to conclude agreements in both the U.S. and in Europe with companies that employ the other major diagnostic technology—flow cytometry, which detects hematologic diseases such as leukemia using blood or body fluids, rather than tissue.

As a part of the strategic development plan for Campath, ILEX recently acquired exclusive commercial rights to CD52 antigen testing worldwide from BTG International Limited. The acquisition followed ILEX studies that employed the technology to explore the expression of CD52 in leukemias and lymphomas.

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Ligand Pharmaceuticals (Nasdaq:LGND) of San Diego said it has completed the restructuring of its Avinza (morphine sulfate extended-release capsules) license and supply agreement with **Elan Corp.** plc (NYSE:ELN).

The agreement improves the gross margin on the treatment and facilitates a co-promotion agreement with a future partner, the company said.

Ligand paid Elan $100 million in return for a reduction in the Elan royalty rate on sales of Avinza by Ligand, rights to sublicense and obtain a co-promotion partner in its territories, and rights to qualify and purchase the treatment from a second manufacturing source, the company said. Elan also has foregone its option to co-promote treatment in the U.S. and Canada.

Royalty and supply price of the treatment for Elan is 10 percent of the product net sales, compared to 30-35 percent in the prior agreement, the company said.

"Our No. 1 priority is to finalize an attractive financial agreement with the best co-promotion partner as quickly as possible to accelerate Avinza market uptake," said David Robinson, chairman, president, and CEO of Ligand.

Under the revised agreement, Elan will continue to manufacture the treatment for Ligand. Ligand is free to qualify a second, non-Elan manufacturing facility for treatment requirements. Ownership of the Avinza NDA will be transferred from Elan to Ligand, with all corresponding post-approval FDA obligations, the company said.

Ligand financed the restructuring by offering about $135 million of five-year, 6 percent, convertible subordinated notes to qualified institutional buyers pursuant to the exemption from registration provided under Rule 144A of the Securities Act of 1933, the company said. UBS Warburg, the initial purchaser of the notes, also exercised its overallotment option to acquire an additional $20.25 million of notes. The Ligand net proceeds from the offering were approximately $150 million, $100 million of which has been paid to Elan.

Ligand has not yet paid Elan for the 2.2 million Ligand shares it has agreed to purchase from an affiliate of Elan for $9 a share, the company said. Closing of the purchase may occur up to 90 days from the date of the agreement. Elan also has agreed to a six-month lock-up period on 11.8 million of its remaining 12.2 million Ligand shares, and to changes in its registration rights to facilitate an orderly distribution of its shares after the lock-up period.

In March, FDA granted marketing approval for Avinza for the once-daily treatment of moderate-to-severe pain in patients who require continuous, around-the-clock opioid therapy for an extended period of time, the company said. The treatment was developed by Elan, which licensed the U.S. and Canadian rights to Ligand in 1998.

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Mercury Therapeutics Inc. of Woburn, Mass., said it has acquired exclusive rights to a drug target in oncology from **Massachusetts General Hospital**.

The technology will be used by the company to develop small molecule inhibitors to the Ras-Raf protein interaction, a potential oncology drug target.

"We are very pleased to have Mercury Therapeutics license the Ras-Raf technology," said Joseph Avruch, lead inventor on the Ras-Raf patents and chief of the Diabetes Unit at Massachusetts General Hospital and professor of medicine at Harvard Medical School. "They have an excellent group of scientists coupled with a robust high throughput screening capability that will enable them to rapidly identify and develop inhibitors of this important drug target. An effective inhibitor of this specific target could have a profound impact on the way cancer is currently treated."

The company filed a patent application on a number of compounds it has identified that inhibit this target.

"Thirty percent of all human tumors harbor mutant Ras proteins, said Neal Birnberg, MTI president and CEO. "Tumors bearing tyrosine kinase oncogenes, another large group of human cancers, all require a functional Ras-Raf interaction to be oncogenic and would therefore also be treatable with a Ras pathway inhibitor. A successful drug against Ras-Raf can revolutionize the treatment of the majority of human cancers, much like Gleevec has done for patients suffering from chronic myelogenous leukemia."

In another development, MTI reached a milestone in its strategic alliance with Aventis. The multi-year license and research collaboration, established in 2000, is focused on developing small molecule activators of the proprietary drug target, AMP activated protein kinase (AMPK). AMPK activator drugs would be used to treat type 2 diabetes, obesity, and cardiovascular disease. The Company recently reached its second milestone in the development of lead compounds, triggering a third R&D payment to MTI.

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Remedyne Corp., of Santa Barbara, Calif., said it has obtained an exclusive license from the **Regents of the University of California** to the patent rights covering a key immune stimulating technology, which primes the immune system against diseases such as cancer, or other viral and bacterial pathogens.

The University of California owns the patents to this technology, which was originally developed by Darren Higgins and Daniel Portnoy at UC Berkeley.

"This technology has the potential to significantly boost the effectiveness and application breadth of our products and allow our products to compete favorably with other cancer immunotherapies," said Krisztina

Zsebo, president and CEO of Remedyne. "We are enthusiastic about the development status our orally available immune stimulating product line, RemeStim."

In a study published Nov. 8 in Gene Therapy, researchers at Harvard Medical School and London's Hammersmith Hospital reported findings confirming the effects of the licensed technology when challenged by a highly virulent line of melanoma.

"Our experiments confirm that we can utilize aspects of disease-causing bacteria, turning them into disease fighters," said Higgins, who is now assistant professor, Department of Microbiology and Molecular Genetics, Harvard Medical School, and one of the study's authors. "A vaccine utilizing this technology can direct the immune system away from making antibodies and into making 'killer' T cells, the cells that kill tumors or virally infected cells."

* * *

R2 Technology Inc. of Chicago said it has signed a partnership agreement with **Chroma Medical Systems Inc.** for the development of CAD for computed tomography based virtual colonoscopy, sometimes known as CT colonography.

Under the multi-year agreement, Chroma Medical Systems will develop CAD software for the detection of colon cancer, the company said. R2 Technology will license the Chroma colon CAD software for integration into the R2 investigational ImageCheckerCT CAD system. R2 is currently developing CAD and other analytical tools for CT. Initially, the ImageChecker CT system will provide CAD for CT images of the lung, helping clinicians not only with detection of lung nodules, but with tools to enhance their workflow as well. Other CT applications, such as colon, and other modalities, like projection chest, are planned to follow in subsequent releases.

The ImageChecker CT display workstation is a combination of dedicated computer software and hardware, providing tools for radiologists to aid in the review of CT exams, the company said. The workstation receives CT exams and DICOM structured reports of CAD-identified areas using DICOM protocols. After review of each exam, radiologists can view screens that summarize their findings, and save to a local database in the workstation for later review.

* * *

Triton BioSystems Inc., of Chelmsford, Mass., and **Thermonix Inc**., of Minneapolis, Minn., have merged operations to focus on pre-clinical product development of their Targeted Nano-Therapeutics system for advanced breast cancer.

Under the terms of the merger, the combined companies will continue as Triton BioSystems Inc., with Samuel Straface as CEO. The two companies have independently pursued the development of therapeutics based on non-invasive inductive heating of prosthetic devices and injectable targeted-nanomaterials.

"Combined, we possess stronger intellectual property and know-how to pursue the Targeted Nano-Therapeutics system for cancer as well as a much accelerated product development effort," said Straface. "We believe this merger will leverage existing partnerships and development activities to expedite our path to human clinical trials in 2004, starting with breast cancer."

The Targeted Nano-Therapeutic system consists of magnetic nanomaterials bound to monoclonal antibodies (which, combined, are referred to as bioprobes) and a device capable of generating a magnetic field. An injection into a patient's bloodstream will release millions of bioprobes, each many times smaller than a cancer cell, where they will detect the unique chemical signature of a cancer cell and attach themselves to the cell's surface, the company said.

The payload of nanomaterial then sits ready for the doctor to activate at will. By applying magnetic field energy through the patient's body, the doctor chooses the time to energize the bioprobes, which will selectively kill the cancer cells. The magnetic energy activates the bioprobes by rapidly heating them, thus killing adjacent cancer cells without damaging healthy tissue or organs.

Approvals & Applications:

FDA Approves Taxotere For First-Line Against NSCLC

(Continued from page 1)

The most common severe side effects associated with Taxotere include low white blood cell count, fatigue, fluid retention and mouth sores. The most common non-severe side effects included hair loss, neurosensory, cutaneous, nail changes, nausea and diarrhea. These side effects are generally reversible and manageable. A premedication regimen with corticosteroids is recommended in order to prevent or reduce hypersensitivity and fluid retention.

Taxotere is not appropriate therapy for patients with significant liver impairment or a low white blood cell count.

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Merck & Co. Inc. of Upper Gwyned, Penn., said FDA has assigned a six-month priority review to its new drug application for Emend (aprepitant), an investigational Substance P neurokinin-1 receptor antagonist studied in combination with other anti-emetic agents for the prevention of chemotherapy-induced nausea and vomiting.

The application includes results from seven safety and efficacy studies that evaluated the once-daily, oral medicine in combination with other anti-emetic drugs in patients with acute (0 to 24 hours) and delayed (2 to 5 days) nausea and vomiting associated with single and repeated courses of highly emetogenic chemotherapy, including cisplatin, the company said.

Merck researchers have been studying investigational agents that block the binding of Substance P to NK-1 receptors in the brain and gastrointestinal tract to determine if the agents may inhibit the nausea and vomiting frequently induced by anti-cancer medicines, the company said.

Emend is a registered trademark of Merck & Co. Inc. Platinol-AQ (cisplatin injection) is a registered trademark of Bristol-Myers Squibb Co.

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MGI Pharma Inc. (Nasdaq:MOGN) of Minneapolis and its partner **Helsinn Healthcare**, of Lugano, Switzerland, said FDA has accepted their new drug application to market palonosetron for the prevention of chemotherapy-induced nausea and vomiting.

The NDA included clinical data from completed phase III trials of the treatment in both moderately- and highly-emetogenic CINV, the companies said.

The acceptance for review indicates that the NDA is sufficiently complete to permit a substantive review, the companies said. The filing of the application by the FDA does not represent any opinion regarding the safety, efficacy, or approvability of the product. Under the PDUFA III (Prescription Drug User Fee Act), the FDA would review and act on the NDA within 10 months of receipt.

"Pending FDA approval, MGI would launch palonosetron in the U.S. in the second half of 2003," said Lonnie Moulder, president and chief operating officer at MGI Pharma.

Palonosetron is a selective 5-HT3 receptor antagonist with receptor-binding affinity and an extended plasma half-life. Clinical studies to date have demonstrated that it was well-tolerated and adverse events were similar to currently marketed 5-HT3 antagonists, with the most common being mild to moderate headache and constipation, the companies said.

The companies said they had achieved primary endpoint in the phase III trials in April, based on preliminary analysis of the data.

The North American market for 5-HT3 antagonists is over $1 billion, and includes the CINV prevention and treatment market which is about $800 million, the companies said.

Oncology Management:

New Firm Offers Oncology Market Analysis Software

Strategic Answers Inc. of Toronto, Boston, and San Francisco, said it offers an information package for providing a competitive advantage for companies with an interest in novel oncology drugs.

OncoAnswers.com consists of OncoEdge, the company's software model designed to assist pharmaceutical and biotech companies in the market potential analysis of specific oncology-related opportunities. The model incorporates tumor-specific patient demographics, competitive intelligence, staging and survival data, as well as trends in cancer incidence and mortality to assess the commercial revenue opportunity for a particular oncology drug in any country, the company said.

OncoAnswers.com also includes OncoInsights, the company's information on physician advisory panel reports and other publications, highlights and interpretations about major oncology meetings and conferences, new drug approvals, links to and ranking of relevant Web sites, impact of key clinical trials, reimbursement highlights, and SAI's Partners' insights.

SAI was founded earlier this year by pharmaceutical alumnae Bernie Manente, Stephanie Mazzei, Don Stark, and Sandi Yurichuk.

SAI's core business is to gather, analyze, quantify and validate information about various diseases in order to assist pharmaceutical and biotech company clients in making strategic decisions to support their commercial efforts.

* * *

Stentor Inc., of San Francisco, said the

University of Texas M. D. Anderson Cancer Center, of Houston, has integrated the iSite 3.0 complete digital imaging system.

iSite 3.0 is an enterprise PACS that enables hospitals to eliminate the need for film by providing instant enterprise-wide image distribution, advanced radiology workstations and always online long-term storage.

"Stentor's iSite 3.0 makes it easy and efficient to view, distribute and store diagnostic-quality digital medical images," said Kevin McEnery, associate professor of radiology and associate division head for informatics of diagnostic imaging at M.D. Anderson. "iSite has proved to be an invaluable tool for our clinical and radiology staff, enabling collaboration and smoother workflow, and ultimately helping improve patient care. The iSite system provides a solid foundation for the transition to filmless patient care."

M.D. Anderson began implementing iSite Enterprise, Stentor's Web-based enterprise-wide image distribution system, in 2001 and has since brought more than 350,000 patient studies and 25 million images online.

Clinical Trials:

Adherex To Begin Phase I Trial Of Exherin At Ottawa Center

Adherex Technologies (TSX:AHX) of Ottowa, Canada, said Health Canada approved its clinical trial application for the compound Exherin for cancer.

"Over the past year, we have successfully completed the pre-clinical development of Exherin, including formulation and manufacturing, pharmacology and toxicology studies and clinical protocol design," said Robin Norris, president and chief operating officer of Adherex.

Exherin, an angiolytic, causes tumor blood vessels to rupture and slows or stops the flow of blood to cancer cells, the company said.

The phase I trial will begin before the end of 2002 at the Ottawa Regional Cancer Centre, the company said.

* * *

Marshall Edwards Inc. (LSE-AIM: MSH) said Yale University School of Medicine has begun a phase II trial of phenoxodiol for recurrent ovarian and fallopian cancers.

The trial is part of a multi-center, multi-national study, the company said. Thomas Rutherford, associate professor of gynecologic oncology and Gil Mor, associate professor of obstetrics and gynecology will lead the trial.

The 40 enrollees will receive phenoxodiol by intravenous injection on two consecutive days per week for a treatment cycle lasting 12 weeks, the company said. The clinical endpoints will include tumor mass, tumor markers, and one-year survival.

Phenoxodiol kills cancer cells by inducing apoptosis, the company said.

* * *

Dendreon Corp. Nasdaq:DNDN) of Seattle said following discussions with FDA, the company will amend the protocol for its phase III trial (D9902) of Provenge to enroll only advanced hormone resistant prostate cancer patients with a Gleason score of 7 or less, the population shown to benefit most from the treatment in the first phase III trial (D9901).

The D9902 trial, as amended, will be the trial for seeking marketing approval for the treatment, the company said.

"We believe that amending our phase III protocol in trial D9902 will be the most expeditious way to verify the safety and efficacy of Provenge and to progress in our efforts to make it available to the many prostate cancer patients who might benefit from this therapy," said David Urdal, president and chief scientific officer of Dendreon.

Results from the first double blind, placebo-controlled phase III trial of Provenge demonstrated benefit for hormone resistant prostate cancer with a Gleason score of 7 or less, the company said. In that group of patients, the placebo group had a median time to disease progression of 9 weeks, compared to 16 weeks in the Provenge treated group, with a p-value of 0.002 and a treatment effect of 78 percent. Patients receiving Provenge whose disease had not progressed six months after randomization had a greater than eight-fold advantage in progression-free survival compared to the patients who received placebo (34.7 percent of Provenge patients versus 4 percent of placebo patients).

The most common side effects were chills and fever, which were most often infusion-related and were temporary, with most resolving within 24 hours, the company said.

Final Issue For 2002

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