THE CANCER LETTER

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

NEJM Does About-Face, Issues Correction On CT Lung Cancer Screening Study

By Paul Goldberg

The New England Journal of Medicine published a correction, a clarification, and an editorial addressing the conflicts of interest that were not disclosed by a group of researchers who advocate computed tomography screening for lung cancer.

The corrective actions taken by the NEJM on April 2 represent an about-face in the handling of the controversy over publication of a paper by the International Early Lung Cancer Action Program.

Earlier, the journal's editors argued that the I-ELCAP leaders Claudia Henschke and David Yankelevitz, both of Weill Cornell Medical College, had properly declared their conflicts, but the editors deemed these not relevant to the paper, which was published in the Oct. 26, 2006, issue of the journal.

Last week, the Journal of American Medical Association similarly

(Continued to page 2)

Capitol Hill:

House Committee Investigates Marketing Practices Of Amgen And J&J For ESAs

By Paul Goldberg

Preparing for a hearing on erythropoiesis-stimulating agents, a House committee has asked Amgen Inc. and Johnson & Johnson to turn over documents related direct to consumer advertising and other controversial marketing practices that were used to promote these controversial agents.

The Subcommittee on Oversight & Investigations of the House Committee on Energy & Commerce has asked the ESA sponsors for proprietary marketing documents as it prepares for a May 8 hearing that will focus on DTC advertising, sources said.

In a letter dated March 31, the committee asks J&J to provide information on the advertising campaign claiming that the company's ESA Procrit could relieve the cancer patients' symptoms of fatigue and improve their quality of life. A letter to Amgen seeks information on DTC marketing of the white blood cell growth factors and the practice of "bundling" of these products with the company's ESA Aranesp.

The hearing will also consider the DTC campaigns for the drugs Vytorin and Lipitor, sources said.

"Millions of dollars have been poured into aggressive marketing campaigns, despite mounting evidence that [ESAs] pose serious risks,"

(Continued to page 6)

Cornell Says Tobacco Money Was Accepted For Public Good

(Continued from page 1)

published a correction related to the research group's undeclared conflicts of interest. Published online on March 24, the correction is attached to a paper that appeared in the July 12, 2006, issue of the journal and a letter to the editor in the Aug. 1, 2007, issue.

JAMA is investigating Henschke's failure to disclose having received $3.6 million from the cigarette maker Liggett. The story about tobacco funding of the group's research was reported concurrently by The Cancer Letter and The New York Times on March 26 and was picked up by television networks and other national news media.

The NEJM correction states that the I-ELCAP disclosure statement should have read: "Drs. Henschke and Yankelevitz report receiving royalties from Cornell Research Foundation as inventors of methods to assess tumor growth and regression on imaging tests for which pending patents are held by Cornell Research Foundation and licensed to General Electric. No other potential conflict of interest relevant to this article was reported."

The NEJM spokesman Karen Pedersen said "the correction we issued today has nothing to do with disclosed or undisclosed patents.

"We learned from the JAMA letter from Henschke on March 24 that there was a financial relationship that existed at the time of publication of our article, which was not disclosed to us," Pedersen said in an e-mail. "The disclosure statement has now been corrected to include that information."

The NEJM editors could not have been shocked by what they saw in JAMA. Henschke and a GE spokesman acknowledged the licensing agreement to The Wall Street Journal. The story, published on the newspaper's Health Blog Oct. 8, 2007, quotes Henschke saying that she had informed the NEJM of the GE royalty agreement, but that the journal decided not to disclose it. The story is posted at: http://blogs.wsj.com/health/2007/10/08/tangled-web-of-conficts-over-lung-cancer-screening/?mod=WSJBlog.

The Wall Street Journal account was cited in the Jan. 18 issue of The Cancer Letter, which revealed that Henschke and Yankelevitz are listed as inventors on one issued U.S. patent and 10 U.S. patent applications for technologies used in CT screening for lung cancer. Worldwide, they are listed as inventors on 27 patents for these technologies.

That story prompted NEJM, JAMA, and other journals to launch investigations of Henschke's conflicts. After looking into the matter, the NEJM editors confirmed Henschke's version of events, stating that "the editors and authors followed standard editorial procedures on disclosure.

"The authors disclosed all potentially relevant information, including patents pending to the editors, and the editors reviewed this information in the light of the content of the article," the NEJM said in a statement received by The Cancer Letter on Jan. 30. "Because it was not considered to be directly relevant to the point of the article, it was not published."

It's unlikely that the correction would be sufficient to put the NEJM in compliance with continuing medical education disclosure requirements, CME experts say. The journal gave CME credit to physicians who read the I-ELCAP paper and answered three questions. The credits were given by the Massachusetts Medical Society, which also publishes the journal.

Patents, licensed or not, represent a conflict under CME rules, and disclosure alone is insufficient to remedy conflicts under these rules (The Cancer Letter, March 14). Officials of the Accreditation Council for Continuing Medical Education said they are investigating. Pedersen didn't respond to a question about CME.

A separate clarification published by the NEJM stemmed from the revelation that Henschke and Yankelevitz had received Liggett money and placed it in a non-profit group that funded I-ELCAP's work. Signed

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

Editorial: 202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016
Letters to the Editor may be sent to the above address.

Subscriptions/Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
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by Henschke, the clarification reads:

"In our article published in the October 26, 2006, issue of the Journal, one of the disclosed sources of funding was the Foundation for Lung Cancer: Early Detection, Prevention and Treatment, which provided partial support for our research. For full transparency we wish to inform you that $3.6 million (virtually all of the Foundation's funding) was contributed in 2000 through 2003 as an unrestricted gift by the Vector Group, the parent company of Liggett Tobacco, which manufactures cigarettes."

Pedersen said that the NEJM had asked Henschke to address this matter in a letter to the editor. "It was not disclosed to us that the Foundation for Lung Cancer: Early Detection, Prevention and Treatment was funded with money from the Liggett group, and we became aware of the association when we were questioned by The New York Times," she said in an e-mail.

In an editorial, the NEJM editors said they were surprised to learn that a non-profit that funded the I-ELCAP study of CT screening was, in fact, dispensing the Liggett money.

"First, as medical journal editors, we believe that it is important that the ultimate source of funding be made clear to the Journal's readers," the editorial reads. "Second, it is appropriate to ask whether a study on clinical outcomes in lung cancer should be directly underwritten in part by the tobacco industry. Given the enormous burden of smoking-related illness and the ongoing sale of cigarettes and other forms of tobacco, one might question the advisability of research entities accepting funding from tobacco companies except through the American Legacy Foundation, which distributes funds received through the Master Settlement Agreement with U.S. tobacco companies.

"We believe that it is important for our readers and the entire biomedical community to be aware of this situation. Our goal is that readers be fully informed about funding sources. It is the responsibility of authors to disclose fully and appropriately the sources of funding of their studies. We expect that authors will be particularly attentive to transparency in reporting if a funding entity has a vested interest in the outcome. The public's trust in biomedical research depends on it."

Second Round of Inconsistent Disclosure

The corrected disclosure published by JAMA online on March 24 appears to be inconsistent with the disclosure Henschke made to the American Cancer Society journals Cancer and Cytopathology.

Henschke's disclosure letter to ACS is posted at http://www.cancerletter.com/publications/special-reports/Henschkeltr.pdf. An excerpted version of the document has been published by the journals online.

Contributions from the Foundation for Lung Cancer Early Detection, Prevention & Treatment, which received the Liggett money, were disclosed to ACS, but not in a corrected disclosure to JAMA.

Funding from GE and Eastman Kodak Corp., which make CT scanners and film, were similarly noted in the letter to ACS but not given to JAMA.

Other apparent omissions from the JAMA disclosure include two grants from Prevent Cancer Foundation; two NIH grants (R01-CA-633931 and R01-CA-79805); and a grant from the U.S. Department of Energy.

Also not listed is funding from the American Legacy Foundation; the Flight Attendants' Medical Research Institute; the City of New York Department of Health and Mental Hygiene; New York State Office of Science, Technology and Academic Research; American Cancer Society; Israel Cancer Association; the Starr Foundation; The New York Community Trust; The Rogers Family Fund; Foundation for Early Detection of Lung Cancer Dorothy R. Cohen Foundation; Research Foundation of Clinic Hirslanden; Yad-Hanadiv Foundation; Jacob and Malka Goldfarb Charitable Foundation; Auen/Berger Foundation; Princess Margaret Foundation; Berger Foundation; Tenet Healthcare Foundation; Ernest E. Stempel Foundation; Academic Medical Development Corp.; Empire Blue Cross and Blue Shield; Weill Medical College of Cornell University; Cornell University; New York Presbyterian Hospital; Clinic Hirslanded; Swedish Hospital; Christiana Care Helen F. Graham Cancer Center; Holy Cross Hospital; Eisenhower Hospital; Jackson Memorial Hospital Health System; Evanston Northwestern Healthcare.

According to the disclosure made to ACS, but not mentioned in JAMA, Yankelevitz also had five research contracts with pharmaceutical companies, manufacturers of medical devices, and the government:

1) AstraZeneca on tumor evaluation, assessment of emphysema, molecular markers of tumor response, starting in 2006; 2) OSI Pharmaceutical for evaluation of tumor response starting in 2006; 3) GlaxoSmithKline for evaluation of tumor response starting in 2006; 4) Visiongate to perform computed optical tomography starting in 2007; and 5) an NCI STTR grant on computer assisted targeting of pulmonary nodules in 2007.

The JAMA disclosure mentions that Henschke "reported receiving compensation for serving as a member of an NCI study section." This was not

mentioned in the disclosure made to ACS.

Research funding is usually listed in a separate section of disclosure in papers published by JAMA. While the 2006 I-ELCAP paper in the journal didn't contain disclosure of funding support, other original research papers in the same issue contained such acknowledgments.

Weill Cornell officials didn't respond substantively to questions from The Cancer Letter. "I could say that I … am concerned about your consistent failure to write a fair and balanced article on the subject, but I won't… I'll think about it," Weill Cornell spokesman Jonathan Weil said in an e-mail to this reporter.

The JAMA editors declined to comment on the latest discrepancies brought to their attention. In what appears to be a similar case of failure to disclose in 2006, JAMA Editor-in-Chief Catherine DeAngelis wrote:

"[Since] the late 1980s, our policy has required *complete* disclosure of all financial interests and relationships and all affiliations relevant to the subject matter discussed in the article…. As recently discussed, JAMA will now require that authors include disclosure of all potential conflicts of interest in the manuscript at the time of submission. Authors should always err on the side of full disclosure and should contact the editorial office if they have any questions or concerns about what constitutes a relevant financial interest or relationship.

"As in the past, we will continue to evaluate all cases very seriously in which authors fail to fully disclose their conflict of interest information; not only will we continue to correct the literature, but we will continue to take additional necessary action based on the results of that evaluation."

"A Grand Plan And Vision"

As they faced press questions stemming from revelation of Liggett's support for I-ELCAP's work, Weill Cornell Medical College officials said the $3.6 million in tobacco money represented the beginning of a plan for tobacco companies to underwrite CT screening research.

"The gift was originally made as part of a grand plan and vision on the part of public health and lung cancer advocacy groups and Vector/Liggett to provide screening research centers throughout the country," Weill Cornell said in a statement.

The Liggett gift was placed in a non-profit that lists I-ELCAP leader Claudia Henschke as president and her collaborators David Yankelevitz as secretary-treasurer. Weill Cornell dean Antonio Gotto and former board chairman Arthur Mahon were also on the board.

While research support from the non-profit, called the Foundation for Lung Cancer Early Detection, Prevention and Treatment, was noted in I-ELCAP publications, its true source of funding wasn't.

According to Weill Cornell's statement, the foundation was organized by Henschke and Yankelevitz "and other advocacy-individuals associated with the I-ELCAP program, with the expectation that other major tobacco companies, in addition to Vector/Liggett, would contribute to this national effort."

"The initial decision to establish a foundation was thought by them to be the most appropriate and effective fundraising vehicle to achieve such a national research plan," the statement reads. "It was expected that, if the additional fundraising were successful, representatives of other institutions would be invited to join the Foundation's board. Dr. Antonio Gotto and Arthur Mahon were invited to join the board because the project was centered at Weill Cornell."

Speaking with a Time reporter, Gotto said that the idea for the foundation originated at a meeting "some time in the late 1990s in which Henschke, representatives from the American Cancer Society and the National Cancer Institute as well as anti-smoking activists were present."

"We made a public announcement along with Liggett that they were making a gift to Weill Cornell to support this activity," Gotto said to Time. "We made no effort to cover up the fact that the money was coming from Liggett. It is patently false that we set up the foundation to cover up the fact that we were getting tobacco money."

The gift from Liggett was announced in the tobacco company's press release, and was covered by USA Today and mentioned in one sentence in a story in Business Week.

Usually, the researcher bears the responsibility to make disclosure, and a hard-to-find press release by a tobacco company and minimal coverage by USA Today don't constitute disclosure, experts say.

"A press release relating to a relationship is not what would be considered common disclosure in academic science, especially if it's coming from the donor and not the recipient," said Eric Campbell, associate professor at Harvard Medical School and Massachusetts General Hospital, who studies the relationships between doctors, drug companies and the Institutional Review Boards. "The more common disclosures are made from the researcher directly to other scientists. Simply issuing a press release that may or may not be found and/or known to anyone, let alone may or may not be printed in

some newspaper, is in my way of thinking, completely inadequate and doesn't follow the norms of disclosure that have been established in science."

Gotto's claim that NCI and ACS officials were at the table at the time when the decision to form the foundation was made is of particular interest to ACS, which has given I-ELCAP over $100,000 over the years. ACS has a policy against commingling of its funds with those obtained from tobacco companies.

The society can't claim that it knew nothing about Henschke's tobacco funding. One of its spokesmen is quoted in a Dec. 4, 2000, story about the Liggett gift. "If it's going to tell people who are smoking they don't have cancer so they can keep smoking and come back to get scanned next year, that's a detriment to public health," ACS spokesman Rachel Tyree said to USA Today. "We must be cautious until we know what their motives are."

Greg Donaldson, ACS vice president, corporate communications, described this statement as appropriately skeptical and reasonable. "In 2005, five years later, we began formally asking grantees and those receiving contract funding from the Society to disclose in writing any potential conflicts and specific tobacco-related funding sources," Donaldson said in an e-mail. "At that time—again, five years after the Liggett gift was publicly announced—the investigator in question acknowledged in writing that there were no such conflicts and that she had no tobacco sources of funding. She has signed several similar documents to that effect in years since."

Donaldson said he has "no knowledge of or record of any meetings where the society was present and wherein those associated with I-ELCAP disclosed tobacco funding and/or related potential conflicts. We are currently revisiting and reviewing Society policies and procedures related to seeking such funding disclosures, monitoring and, when necessary, enforcing them.

"In the mean time, we have taken steps to eliminate all perceived ties with the investigators associated with this particular trial and, by extension, any questionable sources of funding," Donaldson said.

Lung Cancer Alliance Offers Unwavering Support

The Lung Cancer Alliance, a Washington group that lobbies to change the practice of medicine to include CT screening, said it continues to support Henschke.

"Sadly, this is far from the truth, and another attempt to discredit I-ELCAP and lung cancer screening in general," Laurie Fenton-Ambrose, LCA president and CEO, said in a statement. "Why else raise this now? The donation was made eight years ago, was publicly reported, and was an unrestricted grant that allowed for no control by the donor. We will not let those who want to deny the lung cancer community the benefits they deserve defeat our efforts."

The defense of a tobacco company's support for the I-ELCAP study requires a delicate balancing act for Fenton-Ambrose, who had previously criticized the investigators of the NCI-sponsored randomized National Lung Screening Trial of acting as expert witnesses for tobacco companies in trials where plaintiffs demanded CT screening as part of damages assessed against tobacco companies.

Only one of the two scientists—Denise Aberle, co-principal investigator of NLST and professor of radiology at the David Geffen School of Medicine at UCLA—testified in such a case, arguing that the value of CT screening for lung cancer remains unproven.

Aberle's institution received $30,750 for her testimony, transferring $11,576, into Aberle's professional academic account, which is used to pay medical association dues, journal subscriptions, and other professional expenses. None of the money went to pay for Aberle's research, documents show.

On June 1, 2007, at the National Lung Cancer Partnership Annual Meeting in Chicago, Fenton-Ambrose publicly confronted Aberle about her testimony.

"Dr. Aberle, this is directed to you, and in all due respect, because you have such stature and integrity, I need to ask you about your work as an expert witness in class action lawsuits on behalf of Big Tobacco," she said at the question and answer session that followed Aberle's point-counter-point with Henschke.

"I wonder if you could address this and assure us that this poses no conflicts of interest, because you have such credibility," Fenton-Ambrose continued. "I would hate to see tobacco interests benefiting from that."

Aberle offered to answer the question off-line, but her answers didn't preclude Fenton-Ambrose and other Henschke supporters from seeking a Congressional investigation of NLST (The Cancer Letter, Oct. 26, 2007). The status of that investigation is uncertain.

On March, 24, The New York Times reporter Gardiner Harris asked Fenton-Ambrose to distinguish Aberle's alleged conflict from Henschke's acceptance of a much larger sum of Liggett money to fund I-ELCAP research. The exchange didn't end up in the story, but Fenton-Ambrose's response, in a letter to Harris, was posted on the LCA website.

The text of Fenton-Ambrose's letter follows:

Dear Gardiner,

Last week you asked me why we were concerned about a researcher taking money from tobacco companies for "giving an opinion" in a lawsuit involving screening and not concerned about tobacco money being used for independent research on screening.

Let me reiterate my response. There is an enormous difference.

Tobacco companies do not pay for testimony unless it would be advantageous to them. Tobacco companies have a long and sordid history of manipulating science and research, as well as scientists, researchers and doctors, to protect their interests. In this case, they got what they paid for. The testimony was not unbiased. The witness is highly critical of screening, which is described as "reckless" and "may kill a lot more than lung cancer will."

The witness testified for and received payments from the three largest tobacco companies in a deposition in 2000 and in open court in 2003, during which time frame this same witness was receiving federal funding to design and run a $225,000,000 trial on the efficacy of CT screening. Testifying for either side in the lawsuit would be inappropriate. Testifying on behalf of big tobacco companies and receiving payment from big tobacco for doing so, is an outrageous abuse of the witness's federally financed position as arbiter in a screening trial whose outcome could be the determining factor in screening liability suits not just in the US but around the world.

The distinction between that activity and the Cornell Weill research gift is wonderfully clear. In 1997, Liggett publicly admitted they and all the tobacco companies had known but covered up that smoking caused lung cancer. The breaking of ranks and release of key documents led to the $250 billion Master Settlement Agreement that has funded, among many things, many cancer and disease research programs around the country. Are you questioning these tobacco funded research programs as well?

In 2000, Vector Ltd., whose holdings included Liggett, publicly announced a $2.4 million unrestricted gift for lung cancer screening research. This was openly discussed at meetings, advocated for by LCA's management and was widely reported in the media. It is my understanding that it was given to a foundation within Cornell Weill, the only consortia at that time doing early detection research, to help advance screening research at institutions around the world. And it was set up to prevent big tobacco from controlling or manipulating this research to their advantage. At this time, many in the public health field were calling for penalty payments from big tobacco in an attempt to right the human tragedy and social costs brought about by big tobacco's conduct.

Indeed, this has been LCA's long held position as reinforced as recently as 2005 when we filed our Amicus Brief before the U.S. Court of Appeals asking that, in addition to the prevention and cessation remedies sought by the federal government and other public health interveners, that penalty payments to fund independent research for early detection and better treatments also be included as a remedy. LCA's long held position is that big tobacco's deceitful marketing and cover-up of tobacco's harms has lead directly to the underfunding of lung cancer research. Is seeking these and other penalty payments to advance research to help victims then wrong?

Lastly, I continue to be concerned that lost in these various questions and comments is any understanding of the public health epidemic upon us. Lung cancer is the most lethal of all cancers—killing more people than breast, prostate, colon, liver, kidney and melanoma cancers combined—85% of which are current and former smokers—most of whom will die within a year of diagnosis because their cancers are found too late. We can help those at high risk for lung cancer today through the use of CT scans—and we stand proudly with those in the public health community who view lung cancer as a disease deserving of increased compassion

Capitol Hill:

House Committee To Examine ESA Marketing Practices

(Continued from page 1)

committee Chairman John Dingell (D-Mich.) said in a statement. "These potentially harmful drugs are over-prescribed and widely used off-label, and it's time we evaluate the marketing practices used to push them."

"Patients are placed in danger when direct-to-consumer advertising highlights the benefits but not the life-threatening risks associated with a drug," said the Oversight & Investigations Chairman Bart Stupak (D-Mich.). "In this case, the advertising seems to have fueled off-label uses of EPO products, exacerbating the risk to patients."

DTC Marketing of Procrit

"We understand that J&J has discontinued both television advertising for Procrit and advertising in general circulation periodicals," the letter to J&J states. "Nevertheless, this committee is concerned that J&J may

have used misleading direct to consumer television and print advertisements for Procrit to help fuel excessive and dangerous off-label use of the drug, particularly in connection with unsubstantiated 'quality of life' claims."

The committee asks for the following records:

—"All records relating to any television advertisements pertaining to Procrit, including copies of all your television advertisements and their run dates;

—"All records relating to your association with the National Minority AIDS Council and/or the Balm in Gilead in connection with any print advertisements and/or posters featuring former U.S. Surgeon General, Dr. Joycelyn Elders, including copies of all such advertisements and their run dates; and

—"All records relating to future plans for DTC advertising of Procrit."

The committee asks J&J to answer the following questions:

—"How much money did J&J spend in connection with Procrit television advertisements in each year beginning with 2001 to the year in which the last television advertisement was aired?

—"How much money did J&J spend in connection with Procrit print advertisements in each year beginning with 2001 to the year in which the last print ad was published in a general circulation periodical?"

—"Why did J&J discontinue television advertisements for Procrit?"

Bundling of Red & White Growth Factors

"We understand that Amgen has not engaged in DTC product advertising for either Epogen or Aranesp since their launch," the letter to Amgen states. "We are aware, however, that Amgen markets Aranesp to physicians in conjunction with Neupogen and Neulasta, and we are concerned that such 'bundling' practices have helped fuel dangerous off-label use of Aranesp."

The committee asks for the following documents pertaining to the marketing of Aranesp, Neupogen and Neulasta:

—"Copies of your television and print advertisements pertaining to Neupogen and/or Neulasta, including copies of their run dates;

—"Copies of your contracts with oncologists pertaining to the practice of bundlingor offering discounts on the purchase of Neupogen and/or Neulasta to physicians who sell certain amounts of Aranesp; and

—"All records relating to future plans for marketing Aranesp."

The committee asks Amgen to respond to the following questions:

—"Since Aranesp was launched in 2001, how many physicians and/or oncology practices signed contracts pertaining to the practice of bundling or offering discounts on the purchase of Neupogen and/or Neulasta in return for sales/use of Aranesp?

—"Since Aranesp was launched in 2001, how much money has Amgen spent annually in connection with marketing the practice of bundling of sales of Neupogen and/or Neulasta and Aranesp, including costs of DTC advertising for Neupogen and/or Neulasta?

—"Since Aranesp was launched in 2001, how much money has Amgen made annually in connection with the bundling of its sales of Neupogen/Neulasta and Aranesp?"

The letters are posted at http://energycommerce.house.gov/Press_110/index_110.shtml#Letters.

Obituary:

Edwin Fisher, Pathologist And A Leader Of NSABP

EDWIN FISHER, principal pathologist for the National Surgical Adjuvant Breast and Bowel Project for more than 30 years, died March 13 in Florida while undergoing treatment for pancreatic cancer. He was 84 and was a professor of human oncology at Drexel University College of Medicine at Allegheny General Hospital.

Fisher worked with his brother Bernard Fisher in the laboratory doing what would now be called translational research to develop hypotheses about breast cancer treatment that were later tested in clinical trials. Bernard Fisher became chairman of NSABP in 1970 and brought the clinical trials cooperative group to Pittsburgh from Buffalo.

Their work together dramatically changed the treatment of breast cancer from the standard of radical, disfiguring surgeries to breast-preserving operations and radiotherapy.

"The first day I arrived in Pittsburgh in 1973, Bernie Fisher pointed out to me that his brother was more than a pathologist—Ed was a scientist," said Normal Wolmark, NSABP chairman. "He was an integral part of the NSABP, always part of the scientific team. It's so rare to see two brothers working hand-in-hand with the same goals. They were an extraordinary pair."

Fisher continued to work up to the end of his life. "Every time we had a difficult slide, we would send it to him, even when he spent part of the year in Florida,"

Wolmark said. "He worked to the last, with an unfinished manuscript still in his briefcase."

A Pittsburgh native, Fisher graduated from high school in 1941. He served in an Army student training program during World War II. He received a bachelor's degree from University of Pittsburgh in 1945, while he was in medical school. He received his M.D. from University of Pittsburgh School of Medicine in 1947.

He served his internship and residency at Mercy Hospital in Pittsburgh. After a pathology residency at Cleveland Clinic, he served for two years at NIH in the Department of Pathology and Histochemistry.

Fisher returned to Pittsburgh in 1954, becoming chief of laboratory services at the Veterans Administration Hospital. He was also associate professor of pathology at University of Pittsburgh, becoming a full professor in 1958. He remained at Pitt until 1985, when he moved to Drexel.

In 1970, he was named director of laboratories at Shadyside Hospital, a position he held until 1993.

"He was the kind of person who left his mark on everybody," Wolmark said. "He was an extrovert and engaged people. He left the field richer and more advanced for his accomplishments."

NSABP will name its Pathology Laboratory in Fisher's honor.

Fisher is survived by his wife, Carole; two daughters, Marjorie Baum and Abbe Anolik; his brother Bernard Fisher, and three grandchildren. Memorial contributions may be sent to the NSABP Foundation Inc.

In the Cancer Centers:

Burke Elected SGO President

THOMAS BURKE, executive vice president and physician-in-chief at M.D. Anderson Cancer Center, was elected president of the Society of Gynecologic Oncologists at the society's annual meeting last month in Tampa. Burke joined M.D. Anderson in 1988. He is credited with developing conservative surgical options for vulvar cancer, including lymphatic mapping, surgical reconstruction and combined modality therapy for advance tumors. He is head of the Uterine Cancer SPORE grant team at M.D. Anderson. . . . **SIMON POWELL** was named chairman of the Department of Radiation Oncology at Memorial Sloan-Kettering Cancer Center. He will have a joint appointment in the center's Molecular Biology Program. Powell is professor and head of radiation oncology at Washington University School of Medicine in St. Louis. Previously, he was head of the Breast Cancer Service and clinical director of the Gillette Center for Women's Cancers at Massachusetts General Hospital. He also served as co-leader of the Breast Cancer Program at the Dana-Farber Harvard Cancer Center. . . . **ERIC COTTINGTON** was named vice president for research resources management at Memorial Sloan-Kettering Cancer Center. He will oversee the Office of Sponsored Projects, Research Administration, and the Office of Industrial Affairs. Cottington served as the associate vice president for research at Case Western Reserve University, where from June 2000 to February 2008, he was responsible for the Offices of Sponsored Projects and Research Compliance. . . . **CITY OF HOPE** announced an appointment and two promotions. **Robert Powell** was appointed senior vice president of research operations. Powell was associate director of administration at Sylvester Comprehensive Cancer Center at Miller School of Medicine, University of Miami. **Kristine Justus** was promoted to vice president of basic research operations. **Douglas Stahl** was promoted to vice president of clinical research operations. He has been director of the formed Department of Biomedical Informatics since 1998. . . . **MICHAEL LISANTI**, the Margaret Q. Landenberger Professor in Breast Cancer Research at Jefferson Medical College of Thomas Jefferson University and the Kimmel Cancer Center, was named editor-in-chief of The American Journal of Pathology.

Funding Opportunities:

RFA-AI-08-008: Multicenter AIDS Cohort Study, Limited Competition. U01. Application Receipt Date: June 10. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-AI-08-008.html. Inquiries: Rebecca Huppi 301-496-4995; liddellr@exchange.nih.gov.

RFA-CA-08-020: Tumor Stem Cells in Cancer Biology, Prevention, and Therapy. P01. Letters of Intent Receipt Date: June 10. Application Receipt Date: July 10. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-08-020.html. Inquiries: R. Allan Mufson, 301-496-7815; mufsonr@mail.nih.gov.

PA-08-121: Symptom Interactions in Cancer and Immune Disorders. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-08-121.html. Inquiries: Ann O'Mara, 301-496-8541; omaraa@mail.nih.gov.

PA-08-122: Symptom Interactions in Cancer and Immune Disorders. R21. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-08-122.html.

PAR-08-120: Cancer Education Grants Program. R25. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PAR-08-120.html. Inquiries: Lester Gorelic, 301-496-8580; gorelicl@mail.nih.gov.

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THE CANCER LETTER

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Business & Regulatory Report

Drug Companies Agree To Pay $125 Million To Settle Litigation Over Drug Pricing

Eleven pharmaceutical companies agreed to a $125 million settlement in the average wholesale price litigation filed in 2002 by consumers and insurance companies.

The litigation claimed the defendants intentionally inflated reports of the average wholesale prices on certain prescription drugs.

Two defendants, AstraZeneca and Bristol-Myers Squib are not part of settlement.

The published AWP is used to set the price that consumers making Medicare Part B co-payments and Medicare pay for the drug, as well as insurance companies and other third-party payors. The lawsuit contends that consumers and third-party payors paid more than they should because

(Continued to page 2)

Clinical Trials:

Phase III Trial Stopped After Novartis Drug Provides Better PFS In Kidney Cancer

Novartis Oncology said an independent data monitoring committee stopped the Renal Cell cancer treatment with Oral RAD001 given Daily trial, or RECORD-1, a phase III study of the investigational drug everolimus (RAD001) after interim results showed better progression-free survival in advanced kidney cancer with everolimus treatment compared to placebo.

The committee stopped the trial because it met its primary endpoint.

RECORD-1, the largest phase III trial to investigate oral mTOR inhibitor everolimus for metastatic RCC with failed prior targeted therapy, included participants who had their cancer worsen despite receiving treatments such as Nexavar (sorafenib) or Sutent (sunitinib) or both. In addition, prior therapy with Avastin (bevacizumab) and interferon also was allowed.

"This progression-free survival benefit demonstrates the possibilities of continuous mTOR inhibition as a promising target in oncology," said David Epstein, president and CEO, Novartis Oncology. "These data are the first from a broad clinical research program that includes studies in patients with high unmet needs suffering from a variety of cancers. Everolimus is the first compound in our oncology late-stage pipeline with six compounds in registration trials to show exciting clinical data this year."

Randomized for the trial was done according to Memorial Sloan-Kettering Cancer Center risk criteria and prior anti-cancer therapy.

In addition to RCC, everolimus is being evaluated in neuroendocrine tumors, lymphoma, other cancers, and tuberous sclerosis as a single agent

(Continued to page 2)

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

Firms Settle AWP Litigation; Two Companies To Go To Trial

(Continued from page 1)

of the false AWP reporting by the companies.

The settlement includes branded and generic drugs used in cancer treatment, HIV and other illnesses. Under the settlement, 82.5 percent of the fund is designated for third-party claims of payors and the remaining 17.5 percent is for consumer claims.

The defendants include Abbott Laboratories, Amgen Inc., Aventis Pharmaceuticals Inc., Hoechst Marion Roussel, Baxter Healthcare Corp., Baxter International Inc., Bayer Corp., Dey Inc., Fujisawa Healthcare Inc., Fujisawa USA Inc., Immunex Corp., Pharmacia Corp., Pharmacia & Upjohn LLC Sicor Inc., Gensia Inc., Gensia Sicor Pharmaceuticals Inc., Watson Pharmaceuticals Inc., and ZLB Behring L.L.C.

Drugs covered in the settlement include Aranesp, Epogen, Neupogen, Neulasta, Anzemet, Ferrlecit and Infed.

Medicare Part B recipients eligible to participate in the settlement will receive a mailing outlining claim procedures. The class includes anyone who reimbursed any portion of an insured's Medicare Part B co-payment between Jan. 1, 1991 through Jan. 1, 2005 or who made reimbursements outside of Medicare Part B for any of the named drugs from Jan 1, 1991 through March 1, 2008. The court will hold a final hearing to approve all settlement details.

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

Editorial: 202-362-1809 Fax: 202-379-1787
PO Box 9905, Washington DC 20016

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

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Other settlements in the AWP case came in August 2006, when GlaxoSmithKline agreed to a nationwide $70 million settlement and May of 2007 when AstraZeneca agreed to a $24 million settlement to Medicare Part B Zoladex users nationwide. After a trial, the court in November 2007 ordered AstraZeneca and Bristol-Myers Squibb to pay $14 million to insurance companies and consumers in Massachusetts for their roles in unfair trade practices.

The court is expected to set a trial date for remaining claims against AstraZeneca and BMS on behalf of insurance companies and consumers outside of Massachusetts.

Altogen Biosystems of Las Vegas said is has begun Altogen Custom Services, a contract research service for biotechnology and pharmaceutical services, including RNA Interference services, generation of stably-expressing cell lines, assay development, screening and transfection services.

The service would draw upon its hundred cancer cell lines and research in polymer and nanoparticle-based gene delivery technologies.

Altogen Custom Services offers the generation of stable cell lines by transforming the cell line of choice to stably express vector or gene of interest. Optional cloning and shRNA expression services are available.

Clinical Trials:

Novartis Drug Everolimus Provides Better PFS In Study

(Continued from page 1)

or in combination with existing cancer therapies.

Safety findings were manageable and consistent with prior phase II studies. Common adverse events included mouth ulcers, high blood lipids, high blood sugar, skin rash, low red blood count, low phosphate levels, and inflammation of the lungs.

Everolimus, a once-daily therapy, inhibits mTOR, a protein that acts as a central regulator of tumor cell division, cell metabolism and blood vessel growth.

Anadys Pharmaceuticals Inc. (NASDAQ: ANDS) of San Diego said dosing has begun in its phase I study of ANA773, an oral TLR7 agonist prodrug for advanced solid tumors.

The trial is a safety and tolerability study to identify pharmacologically active doses and preliminary antitumor activity as well as to select the dose and schedule for phase II trials, the company said.

The trial, a multiple ascending dose study, would also monitor pharmacodynamic responses indicative of immunological stimulation, the company said. Initially, dosing will occur every other day. Anadys said it also would investigate additional schedules and could have an enrollment of up to 60 patients.

Pharmacology studies demonstrate ANA773 can elicit immune responses and components of the response can be modulated by both dose and schedule of administration, the company said.

Blumenthal Cancer Center at Carolinas Medical Center of Charlotte said it has entered into a partnership with **Moffitt Cancer Center** of Florida for Total Cancer Care, a study of individualized treatments for specific types of cancer.

Over the next five years, CMC said it would enroll more than 2,300 patients. The study would collect tissue samples, medical histories and clinical records.

Total Cancer Care recognizes that there are more than 200 different types of cancer irrespective of where they first appear, the center said. Each type has a specific molecular fingerprint made up of 30,000 genes that could affect how it responds to different forms of treatment. By developing a data base of tissue samples from many cancer types, individualized therapies that target the specific cancer may be designed, avoiding treatments that have little or no effect.

"The Total Cancer Care project is the kind of clinical research that physicians at Blumenthal Cancer Center are seeking for their patients," said Jeffrey Kneisl, medical director of Blumenthal Cancer Center and principal investigator for the Total Cancer Care study at CMC. "This is a thoughtfully conceived, methodically planned project that joins comprehensive cancer centers, cutting-edge research and patient-specific care."

"Our vision is to integrate new technologies into the standard of care and improve outcomes by partnering with outstanding health care institutions," said William Dalton, president, CEO and director of Moffitt Cancer Center.

Dendreon Corp. (NASDAQ:DNDN) of Seattle said FDA agreed to an amended Special Protocol Assessment in the phase III Immunotherapy for Prostate AdenoCarcinoma Treatment, also known as D9902B or IMPACT trial, for Provenge (sipuleucel-T), its investigational active cellular immunotherapy in advanced prostate cancer.

In addition, FDA said it would accept a positive interim or final analysis from the IMPACT trial to amend the Biologics License Application for licensure of Provenge, the company said.

The amended SPA accelerates the timing of the final IMPACT results by one year while maintaining comparable powering of the interim and final results of the study, the company said. By increasing the number of events and decreasing the alpha spending function for the interim analysis, Dendreon said it could reduce the number of events for the final analysis from 360 to 304 and still maintain a comparable statistical power for both the interim and final analyses. Interim results are still expected in the second half of 2008; however, final results are now expected in the second half of 2009 rather than 2010.

Based on the statistical plan in the amended SPA, if the treatment effect at the interim analysis for the IMPACT trial is consistent with the integrated results of the two completed phase III studies (D9901 and D9902A), Dendreon said it would achieve the pre-specified criterion for significance and would amend the BLA submission with FDA based on the interim results.

Genta Inc. (NASDAQ:GNTA) of Berkeley Heights, N.J., said the Data Safety Monitoring Board for AGENDA, a phase III trial of Genasense (oblimersen sodium) Injection has recommended that the trial be continued as originally planned after initial review of blinded safety data from the study.

AGENDA is a randomized, double-blind, placebo-controlled trial that is intended to support global registration of Genasense for patients with advanced melanoma.

The study is designed to confirm the results from Genta's prior randomized trial of Genasense combined with dacarbazine in patients identified by a biomarker who have not previously received chemotherapy.

The co-primary endpoints of AGENDA are progression-free survival and overall survival.

At the end of the first quarter, the trial had accrued approximately 50 patients with approximately 60% of planned investigative sites having been initiated.

Countries with sites currently open for enrollment include the U.S., Canada, Australia, France, Germany, Austria, and the Czech Republic. The trial is planned to open at approximately 90 sites worldwide, and most remaining sites are expected to initiate within the next 30 days. Target accrual of 300 patients is expected to complete in the fourth quarter of 2008, with initial data expected shortly thereafter.

"We believe the current rate, combined with

enrollment from new sites that will open in the near future, should allow us to maintain our timelines for completion of accrual," Loretta Itri, Genta president, pharmaceutical development, said in a statement.

AGENDA employs a biomarker to define patients who derived maximum clinical benefit during a large randomized study of DTIC with or without Genasense, known as study GM301, the company said. These patients are characterized by low- normal levels of LDH (lactate dehydrogenase), a tumor-derived enzyme that is readily detected in blood. Analysis of the previous efficacy outcomes observed in 274 patients from GM301, which AGENDA is designed to confirm, yielded the following results:

In another development, Genta said that in its 2007 financial statements included in the company's annual report on Form 10-K, the auditor's opinion contained a "going concern" qualification. NASDAQ's marketplace rules require NASDAQ-listed companies to publicly announce the receipt of an audit opinion containing a "going concern" qualification.

Nventa Biopharmaceuticals Corporation (TSX**:** NVN) of San Diego said it has completed enrollment and initiated dosing of the fourth and final cohort in its phase I dose escalation trial of new HspE7 (HspE7 + Poly-ICLC, a toll-like receptor-3, or TLR3 agonist) for cervical intraepithelial neoplasia.

The study examines the safety of the agent, an investigational therapeutic vaccine for human papillomavirus-related diseases, the company said.

"We have spent considerable time analyzing the need for a fifth cohort, and have determined that the fourth cohort dose level is likely optimal for future clinical trials," said Gregory McKee, president and CEO at Nventa.

When completed, the trial will have dosed four cohorts totaling 17 patients with a fixed dose of 500 mcg of HspE7 and either 50, 500, 1,000 or 2,000 mcg of the adjuvant, Poly-ICLC, the company said. In addition to safety data, immunological data are being collected pre-treatment, following each dose of new HspE7, and at the end of the study. Patients are also being typed for class I and II human leukocyte antigen subtypes, and are being evaluated for cytokine responses, anti-HspE7 antibodies and cellular immunology.

New HspE7 contains CoVal fusion protein, HspE7 co-administered with the adjuvant, Poly-ICLC, a toll-like receptor-3 agonist adjuvant, the company said. HspE7 is derived from the Nventa proprietary CoVal fusion platform, which uses recombinant DNA technology to covalently fuse stress proteins to target antigens, thereby stimulating cellular immune system responses.

Raven biotechnologies Inc. of South San Francisco said it has begun a phase II study of RAV12 in combination with gemcitabine for metastatic pancreatic cancer.

The study will be conducted at 20 institutions including Fox Chase Cancer Center, the first site, the company said. Eight sites will participate through the clinical trials consortium, the Pancreatic Cancer Research Team.

After an initial dose-escalation run-in segment of 18 patients, the trial will enroll 63 patients in an efficacy segment, the company said. The target dose and schedule of RAV12, 0.75 mg/kg twice weekly, was chosen in a completed phase I/IIa trial of 53 patients.

RAV12 is a chimeric monoclonal antibody directed against a primate-specific glycotope displayed on the surfaces of tumor cells, particularly those of gastrointestinal origin, the company said. The agent is efficacious in human colon, gastric, and pancreatic tumor xenograft models in vivo and is well tolerated in repeat dose primate toxicology studies.

In an another development, Raven biotechnologies Inc., said it has entered into a research collaboration with Leland Chung, director of the Molecular Urology and Therapeutics Program, Department of Urology, **Emory University Medical School** to examine prostate cancer biology, disease progression and subsequent metastasis.

Under the collaboration, Raven said it would provide Emory with its prostate cancer stem cells and with a library of antibodies targeting cancer stem cells to study as diagnostic tools for prognosis and treatment.

Raven said it has developed technologies to isolate cancer stem cells and has established lines of pure cancer stem cells for the most prevalent cancers. The company is using the cell lines and its library of anti-cancer antibodies to test for diagnostic and therapeutic applications.

Deals & Collaborations:

AviaraDx, CMM To Collaborate On Cancer Prognostic Tests

Center for Molecular Medicine of Grand Rapids, Mich., said it has entered into an agreement with **AviaraDx** of San Diego to support three tests for cancer prognosis.

The AviaraDx tests provide greater understanding of the molecular biology underlying tumors, the company said. The test results assist physicians in the management of oncology patients.

Under the agreement, CMM said it would educate physicians on the value and clinical utility of the tests, and coordinate quality-controlled sample preparation and shipping. Analysis of the tumor samples will be handled by AviaraDx in California--a CLIA-certified, CAP-accredited laboratory.

Three tests are available: CancerTYPE ID, H/I (HOXB13/IL17BR) and MGI (Molecular Grade Index), the company said. The CancerTYPE ID test provides a molecular classification of metastatic cancer, pinpointing the organ of origin of the tumor. The H/I test measures a two-gene expression signature and is an independent predictor of treatment outcome for breast cancer patients receiving endocrine therapy; Lastly, the MGI test is a five-gene tumor grade signature which discriminates between tumor grades 1 and 3 and is able to reclassify Grade 2 tumors as Grade-1 like and Grade 3-like, the company said.

The AviaraDx cancer tests are a complement to the Veridex CellSearch tests, the company said. While the AviaraDx tests will be used in the earlier stages of diagnosis and treatment, the CellSearch System is used for more advanced metastatic colorectal, breast and prostate cancer.

Center for Molecular Medicine is a joint venture between Spectrum Health of Grand Rapids and Van Andel Institute.

Caraco Pharmaceutical Laboratories, Ltd. (AMEX:CPD) of Detroit said it has launched amifostine for injection 500mg on behalf of **Sun Pharmaceutical Industries Ltd.**

The product has been added to Caraco's marketing agreement with Sun Pharma.

Sun Pharma recently received FDA approval for its Abbreviated New Drug Application (for generic Ethyol, and being the first-to-file an ANDA with a Paragraph IV certification, has a 180-day marketing exclusivity. Sun Pharma is involved in patent litigation with MedImmune Oncology Inc. concerning this product in the U.S. District Court for the District of Maryland.

Amifostine is indicated to reduce the cumulative renal toxicity associated with repeated administration of cisplatin in patients with ovarian cancer. The product is bioequivalent to Ethyol, a registered trademark of MedImmune Oncology, Inc. Ethyol had U.S. sales of approximately $80 million last year.

EUSA Pharma Inc of Oxford, U.K., said it has entered into a definitive agreement to acquire outstanding shares of **Cytogen Corp.** (NASDAQ: CYTO) of Doulestown, Penn., for $22.6 million.

To meet the acquisition consideration, and fund further investments, EUSA Pharma said it has raised $50 million in an investment round, led by TVM Capital, a venture capital firm.

"The acquisition of Cytogen is of great strategic importance for EUSA as it completes the building of our transatlantic commercialization infrastructure, as well as fitting perfectly with our focus on oncology and pain control," said Bryan Morton, chief executive of EUSA Pharma. "Over the last 18 months EUSA has built a strong European organization covering over 20 countries and marketing a portfolio of six specialty pharmaceuticals. The Cytogen products and U.S. infrastructure are the ideal complement to our business, offering us the opportunity to commercialize a rapidly growing portfolio of medicines on both sides of the Atlantic."

The acquisition of Cytogen brings to the EUSA group an established U.S. commercial organization with a 40-strong specialist oncology sales force and three marketed products, the company said.

The marketed products include Caphosol, a supersaturated calcium phosphate rinse for oral mucositis and xerostomia; ProstaScint, a monoclonal antibody-based agent for prostate cancer; and Quadramet, a radiopharmaceutical for metastatic cancer pain that has spread to the bones, the company said.

Under the merger agreement Cytogen shareholders will receive $0.62 per share, representing a 35 percent premium on the share price at the close of trading on 10 March 2008, and valuing the company at $22.6 million, the company said.

EUSA Pharma said it is a transatlantic specialty pharmaceutical company that in-licenses, develops and markets late-stage oncology, pain control and critical care products.

Genmab A/S (OMX: GEN) Copenhagen and **PDL BioPharma Inc.** (Nasdaq: PDLI) of Redwood City, Calif., said they have closed a transaction under which Genmab has acquired the PDL antibody manufacturing facility of Brooklyn Park, Minn., for $240 million in cash.

Poniard Pharmaceuticals Inc. (NASDAQ:PARD) of South San Francisco announced an agreement with W.

C. Heraeus GmbH for the commercial manufacture and supply of picoplatin active pharmaceutical ingredient.

Poniard is investigating picoplatin in four clinical trials, including the ongoing phase III trial in small cell lung cancer, and is developing picoplatin as a potential new platform product for the treatment of solid tumors.

Under the agreement, Heraeus will manufacture picoplatin API to meet cGMP requirements, and be ready to ship commercial quantities of picoplatin by 2009. Heraeus is the current manufacturer of picoplatin API for the Company's four ongoing clinical trials.

Picoplatin is a chemotherapeutic agent with an improved safety profile compared to existing platinum-based chemotherapeutics, the company said. It was designed to overcome platinum resistance associated with the treatment of solid tumors. Picoplatin has been evaluated in more than 750 patients and has anti-tumor activity in multiple indications, with less severe kidney and nerve toxicity than is commonly observed with other platinum chemotherapy drugs.

Poniard is evaluating intravenous picoplatin in a phase III trial, known as SPEAR (Study of Picoplatin Efficacy After Relapse), in small cell lung cancer. The trial is being conducted under a Special Protocol Assessment FDA with overall survival as the primary endpoint. The Company also is evaluating intravenous picoplatin in phase II trials for the treatment of hormone refractory prostate cancer and metastatic colorectal cancer. Oral picoplatin is being evaluated in a phase I trial in solid tumors.

Sangamo BioSciences Inc. (NASDAQ:SGMO) of Richmond, Calif., said it has entered into a second research and license agreement with **Genentech Inc**. to include additional targets for production cell lines using the Sangamo proprietary zinc finger DNA-binding protein nuclease technology.

"Under the second non-exclusive, research and commercial license agreement, Sangamo will design and engineer additional ZFNs that target genes identified by Genentech to improve protein pharmaceutical production in mammalian cells," said Edward Lanphier, president and CEO of Sangamo. "This further agreement strengthens our belief that there is a growing appreciation of the value of our technology which provides a rapid, reliable and highly specific method to efficiently alter genes in eukaryotic cells."

ZFPs are naturally occurring transcription factors in organisms from yeast to humans, the company said. Transcription factors, which are found in the nucleus of every cell, bind to DNA to regulate gene expression. Though there are many kinds of transcription factors, only ZFPs are amenable to engineering and precise targeting to a particular gene or genes of interest. ZFNs are engineered forms of ZFPs that also contain a nuclease component, which can induce modification of a target gene of interest, the company said.

Siemens Healthcare of Malvern, Pa., said **University Clinic of Schleswig-Holstein** commissioned a consortium of bidders, including Siemens, Bilfinger Berger and HSG Technischer Service, to construct and operate The Competence Center for Radiotherapeutic Oncology, the first particle therapy center in Kiel, Germany.

With overall costs of 250 million euros, this is the largest public-private partnership in the German healthcare sector, the company said.

Set to open in 2012, the PTC would serve the entire Southern Scandinavian region. In its final stage of completion, the three rooms would treat 3,000 patients with particles per year, the company said.

The contract concluded between the consortium of bidders and the UC S-H includes the financing, construction, technical operation, and maintenance of the particle therapy facility in a public private partnership over a period of 25 years, the company said. To implement the project, the sponsors, Siemens Project Ventures and Bilfinger Berger Project Investments, established a project company, which will be refinanced through an international group of banks. In addition to the facilities for applying particle therapy, the PTC will also include a department for conventional radiation therapy.

"The Kiel PTC represents a milestone for medical engineering solutions and partnership models in oncology and will set the trend for additional particle therapy centers in Europe and the U.S.," said Erich Reinhardt, CEO of the Siemens Healthcare Sector.

Silence Therapeutics plc (AIM: SLN) of London said it has entered into a collaboration with **AstraZeneca** for the delivery of siRNA molecules.

The deal builds on the Silence Therapeutics expertise in the delivery of siRNA molecules, in particular with the functional systemic delivery of siRNA in vivo using its proprietary AtuPLEX technology, the company said.

The collaboration is independent of the three-year collaboration signed in 2007 to develop siRNA therapeutics against specific targets exclusive to

AstraZeneca, the company said.

Under this agreement, both Silence Therapeutics and AstraZeneca said they would be allowed to commercialize the delivery systems that they develop.

Silence Therapeutics said it would retain the right to sign further delivery deals to capture value from its AtuPLEX delivery technology as well as any improvements to the technology that it generates either independently or as part of this collaboration.

AtuRNAi, proprietary short interfering RNA molecules, have advantages over conventional siRNA molecules as they show increased stability against nuclease degradation, Silence Therapeutics said. In addition, AtuPLEX, its proprietary systemic delivery system, delivers siRNA molecules to targeted diseased tissues and cells, whilst increasing their bioavailability and intracellular uptake.

Walter and Eliza Hall lnstitute of Medical Research of Melbourne, Australia, said Abbott, Genentech, and WEHI have joined in a tripartite research collaboration for anti-cancer drugs.

"This exciting three party research collaboration increases the chance of translating basic scientific research in apoptosis, into targeted cancer therapeutics," said Julian Clark, head of business development at WEHI.

Under the collaboration, the three parties are engaged in a drug discovery research program, with Genentech and Abbott responsible for the development, manufacturing and commercialization of drugs, the groups said. The discovery stage of the collaboration involves an integrated approach using research sites in South San Francisco, the Chicago area, and Melbourne.

"WEHI's first priority is to ensure that cancer patients benefit from the results of our fundamental research and all three parties in the collaboration are committed to the discovery and development of improved cancer treatments that enable patients to live longer and healthier lives," said Suzanne Cory, director of WEHI.

Product Approvals & Applications:

FDA Grants Orphan Status To ActivBiotics Small Molecule

ActivBiotics, of Wellesley Hill, Mass., said the FDA Office of Orphan Products Development has granted Orphan Drug Designation for M40403, an investigational small molecule, for the prevention of radiation or chemotherapy induced oral mucositis.

M40403 mimics the action of a natural component of the cells, the enzyme superoxide dismutase, the company said. Superoxide dismutase has a double pharmacologic effect during the early stages of tissue damage, first through the reduction of inflammation, and secondarily through the decreased rate of apoptosis.

Bioniche Life Sciences Inc. (TSX: BNC) of Belleville, ON, said it has received Fast-Track designation FDA for its therapy for first-line non-muscle-invasive bladder cancer.

The phase III trial compares a formulation of the Bioniche Mycobacterial Cell Wall-DNA Complex Urocidin to standard therapy in non-muscle-invasive bladder cancer at high risk of recurrence or progression, the company said. Scheduled to begin later this year, the study would demonstrate non-inferior efficacy with respect to disease-free survival and fewer toxicities.

This is the second Bioniche phase III trial to receive Fast-Track designation: the registration trial of Urocidin for bladder cancer was designated as Fast-Track in 2006, the company said. That first refractory phase III trial for bladder cancer is ongoing in Canada and the U.S.

"This is an important milestone for our phase III clinical development program with Urocidin," said Graeme McRae, president and CEO of Bioniche Life Sciences Inc. "It highlights the need for a safer and more effective therapy for first-line bladder cancer. FDA recognizes that the approved therapy is less than satisfactory, and wishes to expedite the introduction of new therapies."

Bioniche said it would begin enrollment recruitment for a second 800-patient study in North America, Australia and Europe this year. That trial would be a double-blind, randomized study comparing the agent to standard treatment for non muscle-invasive bladder cancer at high risk of recurrence or progression.

Bioniche said it also would continue enrollment in its first Fast-Track phase III trial with Urocidin. When fully enrolled, the trial will involve 105 patients in North America with non muscle-invasive bladder cancer that is refractory to BCG. The Data Safety Monitoring Committee held its third scheduled quarterly meeting regarding the clinical trial, after which it recommended that Bioniche "continue the trial unmodified until the next scheduled or triggered meeting."

MCC is a sterile mycobacterial cell wall composition that has a dual mode of action: immune stimulation and direct anticancer activity, the company said. It is

formulated as Urocidin for bladder cancer, where it is administered by the intravesical route directly into the bladder, coming into contact with immune system cells and bladder cancer cells. MCC is also undergoing preclinical evaluation for peritoneal carcinomatosis associated with colon and ovarian cancer.

Cephalon Inc. (NASDAQ:CEPH) of Frazer, Penn., announced that FDA has approved Treanda (bendamustine hydrochloride) for Injection for treatment of patients with chronic lymphocytic leukemia.

The Treanda application as a CLL treatment received priority review from the FDA and was approved within six months of the September 2007 submission.

"Patients with chronic lymphocytic leukemia can often live normal lives for many years because of treatments that control the disease over the long-term," said Bruce Cheson, clinical professor of hematology/oncology at Georgetown University School of Medicine. "Treanda is an effective new option that offers a delay in disease progression, an important goal for patients with chronic lymphocytic leukemia."

In a randomized, international, multicenter, open-label pivotal study of 301 treatment-naive patients with CLL, those who received Treanda had better clinical outcomes compared to patients treated with chlorambucil, an FDA-approved chemotherapy for patients with CLL.

According to the company, Treanda patients had a significantly higher overall response (59% of patients responded to Treanda and 26% of patients responded to chlorambucil; $p < 0.0001$). Patients who received Treanda also had a higher complete response rate than those treated with chlorambucil (8% vs. <1%), which means that after treatment with TREANDA, some patients had no signs of disease in their blood.

Treanda patients had a significantly longer progression- free survival (18 months vs. 6 months; Hazard Ratio = 0.27; $p < 0.0001$), meaning the disease did not get worse for a significant period of time. The response to Treanda lasted longer (duration of response) than in patients who received chlorambucil (19 months vs. 7 months). The most common adverse events in the trial were myelosuppression, fever, nausea, and vomiting.

Genta Inc. (NASDAQ:GNTA) of Berkeley Heights said the FDA Center for Drug Evaluation and Research decided the data are not adequate to approve Genasense (oblimersen sodium) Injection for relapsed or refractory chronic lymphocytic leukemia.

In response to an appeal filed by Genta in October 2007, CDER determined that complete response, which was the primary endpoint in the trial, was an appropriate endpoint for assessing efficacy, the company said. FDA also agreed that the endpoint was achieved, and that the results supported the efficacy of the drug. However, CDER concluded that at present there was insufficient confirmatory evidence in the New Drug Application for approval.

CDER recommended two alternatives, the company said. One option is to conduct an additional trial. The other option is to collect additional information on the clinical course and progression of disease from the previous trial to ascertain whether the data contain sufficient confirmatory evidence. Genta said it would pursue both options.

Hospira Inc. (NYSE:HSP) of Lake Forest, Ill., said FDA approved irinotecan hydrochloride injection in the U.S.

The medication is a generic version of Pfizer Camptosar, and is used for colon or rectal cancer where the disease has recurred or progressed following therapy with other treatments.

The Hospira irinotecan product portfolio offers the medication in 40 mg and 100 mg single-dose vials. Hospira said it is also marketing a 500 mg single-dose vial for additional convenience when preparing and delivering larger doses. The company said it packages irinotecan in its proprietary Onco-Tain vials for safe handling.

Supratek Pharma Inc. of Montreal said FDA has granted orphan drug designation to SP1049C for the treatment of gastric cancer.

Last year Supratek Pharma obtained FDA clearance for its Investigational New Drug application for SP1049C for the treatment of metastatic adenocarcinoma of the upper gastrointestinal tract.

Recently Supratek has also reached an agreement with the FDA for the design of SP1049C pivotal phase III study protocol under the Special Protocol Assessment process. A phase III trial will compare SP1049C plus best supportive care versus BSC alone for metastatic adenocarcinoma of esophagus, gastroesophageal junction and stomach who have failed adjuvant or 1st or 2nd line chemotherapy.

Supratek Pharma will direct the clinical development program.

SP1049C is a composition of block copolymers and doxorubicin.