THE CANCER LETTER

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J&J To Eliminate Its Ortho Biotech Unit As FDA Considers Further Limits On ESAs

By Paul Goldberg

Johnson & Johnson is eliminating the separate business unit Ortho Biotech, which has developed the market for erythropiesis-stimulating agents by claiming in direct-to-consumer advertising that they improved the cancer patients' quality of life.

On April 29, the company told its employees that Ortho Biotech would be combined with another J&J company, Centocor Inc., which markets the agent Remicade, a treatment for autoimmune diseases, now the company's highest grossing drug.

J&J will lay off 400 of Ortho's 1,100 employees and move the business

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In the Cancer Centers:

OHSU Receives $5 Million For Laboratories; Simone Heads Univ. of Florida Cancer Center

OREGON HEALTH and Science University received a $5 million gift to establish the James W. Mills Cancer Research Laboratories in the new Biomedical Research Building. The gift comes from **Lori** and **Jen-Hsun Huang** of Los Altos Hills, Calif., in honor of Lori Huang's father who has been treated with Gleevec for chronic myelogenous leukemia since 2001. **Brian Druker**, director of the OHSU Cancer Institute, in collaboration with Novartis, helped develop Gleevec. "It is really difficult to overstate just how much this remarkable gift will advance our work," said Druker, who also is the JELD-WEN Chair of Leukemia Research, a Howard Hughes Medical Institute Investigator and a recent inductee to the National Academy of Science. The Biomedical Research Building was made possible by the half-billion-dollar public-private partnership known as the Oregon Opportunity, which concluded in 2006. . . . **JOSEPH SIMONE** has been named director of the University of Florida Cancer Center for up to two years while the center becomes established and begins a search for a permanent director. The center is part of a new partnership between H. Lee Moffitt Cancer Center and the University of Florida and Shands Hospital. Simone, president of Simone Consulting, is clinical director emeritus of the Huntsman Cancer Institute and the professor emeritus of pediatrics and medicine at the University of Utah School of Medicine. He was director of St. Jude Children's Research Hospital from 1983 to 1992. From 1992 to 1996, he served as physician-in-chief of Memorial Sloan-Kettering Cancer Center.

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J&J Will Continue Litigation Against Amgen Over Bundling

(Continued from page 1)

from its current headquarters in Bridgewater, N.J., to Centocor's headquarters in Horsham, Pa.

Utilization of ESAs has declined by about half over the past year amid concerns about their toxicity and potential for tumor promotion, and additional restriction of the agents' indications is expected as FDA continues to review their label.

"There has been a pretty significant contraction in the market for ESAs," said J&J spokesman Chris Molineaux. "As we've watched that market contract, and as we continue to negotiate with the FDA, in anticipation of further softening of that market, the decision was made to move the Ortho Biotech commercial business and consolidate it with the Centocor business."

Molineux said the name of the new company remains to be determined, though it's possible that the unit would retain a division called Ortho Biotech. About 150 former Ortho jobs would be eliminated in the company's headquarters, and the remainder would be carved out of the sales force. Ortho's president Kim Taylor would step into the job of Centocor president, filling a vacancy left by Neal Fowler, who left the company in March.

On May 8, the Subcommittee on Oversight and Investigations of the House Committee on Energy and Commerce is expected to hold a hearing about direct-to-consumer advertising, focusing in part on the marketing of Ortho's ESA Procrit (epoetin alfa). Taylor is expected to testify at the hearing next week, a company spokesman said.

According to industry data, Ortho sold $2.246 billion worth of Procrit in the U.S. 2005, but sales slipped to $2.064 billion in 2006 due to competition with the Amgen Inc. agent Aranesp (darbepoetin), which is marketed as part of a "bundle" with the white blood cell growth factor Neulasta. At that time, the U.S. sales of Aranesp grew explosively from $2.104 billion in 2005 to $2.790 billion in 2006.

Worldwide, during that period, Procrit sales in oncology dropped from $3.324 billion to 3.180 billion while Aranesp grew from $3.273 billion to $4,121 billion.

Amgen continues to market Neulasta in direct-to-consumer ads, relying on a system of rebates to induce oncologists to offer Aranesp to their patients.

In the past, Amgen's supply contracts required that doctors meet financial targets for Aranesp sales. However, earlier this year, the company changed the supply contract to require that doctors meet proportional targets for Aranesp use. While financial targets can induce doctors to increase the agent's dose, proportional targets are aimed to protect the market share.

Even as Ortho ceases to be a separate unit of J&J, the company will continue to pursue its litigation claiming that Amgen's bundling practice constitutes an unlawful anticompetitive practice, a company spokesman said.

Overall, J&J and Amgen say that utilization of ESAs has dropped by half since safety concerns about the agents emerged last year. During the first quarter of 2008, Procrit sales decreased by 37 percent compared to last year, the company said in its most recent earnings presentation to analysts. At the same time, Remicade grew by 13 percent in the US and 37 percent worldwide.

Remicade's U.S. sales were at $676 million during the quarter, more than double the Procrit sales of $334 million.

"Centocor has a very substantial market with Remicade, which is approved in 15 indications in three therapeutic areas," Molineaux said. "Remicade continues to deliver strong growth, and Centocor is preparing to launch two new products toward the end of this year. Part of the rationale behind this consolidation is to make sure that the resources get applied to these growth agents. We want to make sure that our resources are going where there is growth."

Ortho was founded in 1990, and its biggest product

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after Procrit is Doxil (doxorubicin HCl liposome injection).

If FDA takes the advice it received at the March 13 meeting of the Oncologic Drugs Advisory Committee, it will place restrictions on ESA use in patients who are being treated with curative—as opposed to palliative—intent. Also, the committee recommended excluding breast and head-and-neck cancers from the label and favored a risk mitigation strategy that may include some form of an informed consent (The Cancer Letter, March 21).

At an Amgen earnings call April 24, Roger Perlmutter, executive vice president, research and development, confirmed that FDA has put forth its position on the label.

"We are having discussions with the agency," Perlmutter said. "There was a lot of commentary at the ODAC about the need to have physician discretion. I think there is much more focus on making sure that patients and physicians are adequately informed and that there is a program in place that make certain that that sort of a dialogue has gone on between patients and physicians, and we are focusing a lot on that kind of [risk management] strategies."

CT Screening:
Chabner Calls For Data Audit Of I-ELCAP Screening Study

By Paul Goldberg

Bruce Chabner, clinical director of the MGH Cancer Center of the Massachusetts General Hospital and a member of the National Cancer Advisory Board, became the first cancer expert to call for an audit of data published by proponents of CT screening of current and former smokers.

In an editorial published in the April issue of The Oncologist, a journal he edits, Chabner said the data published by the International Early Lung Cancer Program should be audited, and financial support received by the group should be fully disclosed.

The screening program, headed by Weill Cornell Medical College researchers Claudia Henschke and David Yankelevitz, has received support from the parent company of the Liggett Group, a cigarette maker. Also, Henschke and Yankelevitz are listed as inventors on a series of patents covering lung screening technology.

An excerpt from Chabner's editorial follows:

"There are significant scientific reasons for concern about [the] conclusion that screening prevents deaths due to lung cancer… [The] methodology of their study was flawed. There was no simultaneously studied control group. The results were confounded by lead-time bias; the fact that many of the small cancers did not recur does not prove that the patients, unscreened, would have died of lung cancer. Their survival may or may not have been related to the screening.

"On the other hand, the majority of lesions detected by screening, and requiring diagnostic follow-up, are not cancers. The cost/benefit of CT screening is now the subject of a well-designed prospective trial by the National Cancer Institute and the American College of Radiology Imaging Network; the results are anticipated in two years.

"Clearly, it is too early to accept the conclusions of Henschke–Yankelevitz's work, and a significant pall has been cast over their studies.

"Because of the importance of the I-ELCAP study and the questions raised regarding its results and sources of funding, it would seem to be of highest priority to have an independent audit of the clinical outcomes of the study, and a full disclosure of all sources of support, direct or indirect. It does not appear, from the text of articles published or from the I-ELCAP website, that a comprehensive audit of clinical outcomes (deaths due to cancer, patients censored from the trial, etc.) was performed as part of this trial.

"If anyone questions the importance of full revelation of conflicts of interest, this episode should provide conclusive evidence of its vital role in placing research in context. The Cancer Letter and The New York Times have done an outstanding job of reporting a COI situation that taints the investigators, their medical school, and their published research.

"The repercussions for the lung cancer field, for the journals, and for the individuals involved are likely to be significant. Further investigations of the overt or covert link(s) between tobacco companies and medical research are warranted.

"What was once only smoke has now become a fire."

The editorial, which accompanies two papers on lung cancer screening, is posted at http://theoncologist.alphamedpress.org/

* * *

Nature Clinical Practice Oncology became the latest journal to publish a correction to a paper by Henschke.

The New England Journal of Medicine, the Journal of the American Medical Association, The Oncologist, and the American Cancer Society journals Cancer and Cytopathology have corrected the record to reflect

Henschke's and Yankelevitz's patents, royalties and funding sources.

The correction published in the May issue of the journal reads:

"In the Viewpoint article by Claudia Henschke published in the August 2007 issue of Nature Clinical Practice Oncology, it was not disclosed at the time of publication that the author is a co-inventor on pending patents owned and filed by Cornell Research Foundation (CRF), a subsidiary of Cornell University, which are non-exclusively licensed to General Electric for technology in general diagnostic use involving computer-aided diagnostic methods, including measurement of nodules. A portion of these royalties is distributed to Dr. Henschke and other coinventors pursuant to Cornell policy, which in turn is consistent with the Bayh–Dole Act. None of these technologies were required in performing any of the screenings described in the article nor was the technology discussed."

Cooperative Groups:

NSABP Protests NIH Rejection Of Appeal Over P-4 Study

By Kirsten Boyd Goldberg

A NCI-supported cooperative group has protested NIH's rejection of its appeal of NCI Director John Niederhuber's decision last year to cancel a breast cancer prevention study.

The National Surgical Adjuvant Breast & Bowel Project sought NIH reversal of Niederhuber's decision to cancel its P-4 STELLAR trial that proposed to test letrozole versus raloxifene to prevent or delay breast cancer in healthy women (The Cancer Letter, Aug. 10, 2007).

NCI staff and review committees took 18 months to issue final approval for the trial, but just as it was to have begun in January 2007, Niederhuber told NSABP to stop the trial so that the institute could conduct further review (The Cancer Letter, March 2, 2007).

Last June, NCI officials informed the group that Niederhuber decided not to fund the study, stating that there were "scientific concerns," including "the dangers of introducing these drugs, with their many known side effects" (The Cancer Letter, June 22, 2007).

Raloxifene was approved by FDA last year for reducing the risk of invasive breast cancer in postmenopausal women, based on the results of NSABP's P-2 STAR trial.

In a letter appealing the NCI decision to NIH Director Elias Zerhouni, NSABP Chairman Norman Wolmark argued that the cancellation of the trial "was the result of an unlawful, ad hoc review" that represented "a dangerous and unjustified departure from NCI's formal review and approval process for clinical trials." NCI's concern about adverse side effects of the drugs "is completely at odds with the fact that the NCI's exhaustive review of the P-4 trial, which included NCI's standard extensive consideration of drug safety, resulted in the Jan. 22, [2007] approval of the P-4 trial by the NCI Executive Committee," Wolmark's appeal stated.

Niederhuber's formation of a working group to re-examine the trial after its approval by the NCI Executive Committee and the National Cancer Advisory Board's decision to renew grants that would have provided funding for the study "signal a radical departure from the peer review process, and would replace that process with ad hoc decision-making of little enduring scientific value," Wolmark wrote.

Rejecting NSABP's appeal, an NIH official wrote that the NCI director's action to form the working group was "employed to solicit recommendations" prior to the final funding decision, and "entirely consistent with NIH policy."

"It was during this process that the specific trial was weighed in the context of the field of chemoprevention and the full body of cancer research," according to the letter signed by Norka Ruiz Bravo, NIH deputy director for extramural research. "It was determined that there is much that is already being studied with the classes of agents proposed for the study and that considerable data concerning the significant adverse effects that women taking these agents experience exists.

"While the P-4 study may provide another possible option for women at risk for breast cancer, it was determined that the dangers of introducing these drugs with their many known side-effects outweighs their potential benefits until we are better able to determine who will benefit from these interventions, how compliant women are likely to be with the drug regimens, and what the longer term effects may be," stated the letter, dated Nov. 19, 2007. "Therefore, Dr. Niederhuber concluded that NCI should not commit to the funding of this particular trial given the numerous scientific concerns and competing program priorities."

By law, the institute director has final say on grant funding decision, the letter stated.

"It is important to highlight that all procedural steps in the grant review process are only advisory. The function of advisory councils is described at 42 U.S.C. § 284a, which states, they shall 'advise, assist, consult with, and make recommendations to the Secretary and

the Director of such institute on matters related to the activities carried out by and through the institute and the policies respecting such activities....' The N1H peer review regulations further emphasize at 42 C.F.R. § 52h.7(b) '[e]xcept to the extent otherwise provided by law, recommendations by peer review groups are advisory only and not binding on the awarding official or the national advisory council or board.' Finally, the NIH Grant Policy Statement clearly states, '[t]he TC Director or designee is the official that has the authority to make final award decisions from among those applications receiving a favorable initial review and Council recommendation....The decision not to award a grant or to award a grant at a particular funding level, is discretionary and is not subject to appeal to any NIH or HHS official or board.' "

In addition to scientific merit, the institute has to consider program priorities and the availability of funds in making a funding decision, Bravo wrote. "In sum, the NCI Director has the responsibility to weigh multiple factors in reaching a final decision about what grants to fund," the letter stated. "Based on our review, we do not believe that there is any right of appeal of the NCI Director's decision in this matter."

Bravo's letter is posted at http://www.cancerletter.com/publications/special-reports.

NSABP's Response

In his response to Bravo's letter, Wolmark said that Niederhuber's actions constituted a "departure" from a "science-driven" review process that NCI has historically followed.

The full text of Wolmark's response follows:

Dear Dr. Bravo:

Thank you for your letter of November 19, 2007 responding to the request I submitted last summer on behalf of the National Surgical Adjuvant Breast and Bowel Project ("NSABP"), seeking Director Zerhouni's review of the NCI's decision to cancel NSABP's P-4 Breast Cancer Prevention Trial. The NSABP appreciates the care with which you have written, and particularly your well taken remarks about our project's valued and ongoing collaboration with NCI in the field of cancer prevention. We have some observations to offer in that regard, but we think it is important first to address some of the other points in your letter.

To begin, we must disagree with your conclusion that no appeal is available from the NCI's decision. In its cancellation notice dated June 20, 2007, NCI explicitly directed the NSABP to cease preparations for the P-4 trial under two existing grants that are not mentioned in your letter. The voidance of those funded grants to the extent that they supported work on P-4 was sufficient to trigger review under 42 C.F.R. § 50.404.

Such a reconsideration was and is very much in order. The standard NCI grant review process as you describe it in your letter—in which rigorous peer review is but one purely advisory step toward a decision vested entirely in the NCI Director's discretion—is simply not the science-driven process that NCI has followed historically and that the scientific community has come to expect. It would do a substantial disservice to our shared public health mission to relegate scientific peer review to a footnote in a decisional process driven by other considerations. Indeed, among many other negative consequences addressed at length in our July 20 submission, a purely advisory peer review process which produces results that a single decisionmaker can supplant, for whatever reasons are important to him or her at the time, is not a process with the transparency and predictability necessary to attract the massive commitment of human and economic capital that successful cancer prevention research demands.

Regrettably, moreover, the NCI's handling of P-4 reveals a process that is in practice even less transparent than the one you outline. The "second level of review" by the National Cancer Advisory Board, to which you attribute the concerns animating NCI's denial of P-4, actually was not where this trial came to an end. On the contrary, the NCAB had already approved funding for the P-4 trial when the NCI Director, taking a step beyond the "second level of review" that you describe, convened a "working group" to assist him in revisiting the considered judgment of the NCAB and the underlying peer review process. Your letter does not address this, but the fact is that the deliberations of this group were not open, its membership was neither ideologically balanced nor without conflict of interest, and, respectfully, we cannot agree with you that its activities were consistent with the Federal Advisory Committee Act, let alone with the policies and best traditions of the NIH.

We do not doubt that NCI is faced with difficult funding decisions in a challenging budgetary environment. In this case, however, the ad hoc process initiated by the NCI Director appears to have been employed to reinforce his own funding priorities by recasting scientific evidence that was already carefully evaluated by peer review groups and other highly qualified professionals. For instance, two peer review panels had already determined that the NSABP had

adequately addressed the safety of participants in the P-4 trial. The drugs that were to have been used in the trial, letrozole and raloxifene, secured FDA approval years ago, and their FDA-approved labels indicate that the possible adverse events associated with them are "mild." Anastrozole, a drug almost identical to letrozole, is being used safely and with a high degree of patient compliance in another NCI-approved NSABP trial called B-35. In July 2007, moreover, the FDA specifically approved raloxifene's use for breast cancer prevention, solidifying its earlier determination in December 2006 that the potential benefits of using raloxifene in the P-4 trial outweighed any safety concern for those women who would qualify for participation in the study.

Nonetheless, after the working group was convened and rendered its report, NCI defended its decision not to fund P-4 by stating the very different conclusion that you articulate again in your letter, namely, that there are "well-known dangers" associated with these drugs that outweigh their potential benefits. Whatever the justifications may be for ad hoc proceedings, such proceedings should never be used as they were here, to pronounce broadly on matters that were already addressed in detail and with scientific rigor during peer review. It is unfortunate that, despite all evidence to the contrary, the NCI Director has repeatedly described the P-4 trial drugs as too toxic, unnecessarily alarming the thousands of women who are receiving the drug for approved indications.

For these reasons, we are of course disappointed in the NIH's decision not to review the NCI's cancellation of this truly promising breast cancer prevention trial. The P-4 trial is only one of the reasons we have pursued these issues, however. The other is the NSABP's genuine concern for the future direction of our valued and longtime partner in cancer prevention, the NCI.

This year, the NSABP celebrates its 50th anniversary. Over the past half century, we have entered more than 150,000 patients and participants into clinical studies that changed the treatment of colorectal cancer and revolutionized the treatment and prevention of breast cancer. The supplanting of radical mastectomy by simple mastectomy and then by lumpectomy plus radiation, the use of adjuvant therapy to alter the natural course of breast and colorectal cancer, the use of tamoxifen and raloxifene for the prevention of breast cancer, the dramatic improvement in survival demonstrated with the use of the monoclonal antibody trastuzumab in women with HER2 positive breast cancer—all of these are the direct result of research carried out over the past 50 years by the NSABP. And NCI was there with us every step of the way.

We at the NSABP want very much to see this extraordinarily successful partnership continue throughout our next 50 years. The NSABP Tissue Bank offers one such collaborative opportunity right now.

Currently, the NSABP Tissue Bank houses tumor tissue blocks from more than 70,000 cases of breast and colorectal cancer from patients who have participated in NSABP clinical trials. Microarrays of tissue from all of the key trials are now available in the tissue bank. Serum and lymphocyte samples are also stored on over 30,000 high risk women who have participated in the two NSABP breast cancer prevention trials.

The NSABP Tissue and Serum Banks operate under the principle of completely open access to all investigators, not just NSABP members. Any investigator may submit a concept to conduct research using resources of the bank and our databases of clinical outcomes. All concepts are reviewed by an external scientific review panel and, after approval, the NSABP works with the investigator to develop a final protocol. An example of the success of this program is the OncotypeDX test, which is the first commercially available 21 gene molecular assay used to evaluate prognosis and predict response to therapy in node negative receptor positive. The test was developed and validated using specimens from the NSABP tissue bank. Efforts are well under way to develop a similar assay for stage 2 colon cancer.

The NSABP has established a collaboration with the NCI's Resources Development Branch to distribute microarrays from the B-28 trial. Microarrays from colon cancer studies will also be incorporated into this collaboration. The NSABP stands ready to expand this collaboration with the NCI to allow the resources of our human specimen banks to be even more widely available to the research community.

We at the NSABP urge the NIH and the NCI to consider these comments in the collaborative spirit in which they are intended. We are of course available at your convenience to discuss these issues or any other matters of concern.

NIH News:

Cancer Genome Consortium Aims For Data On 50 Cancers

NIH announced that it has joined with research organizations from around the world to begin an International Cancer Genome Consortium, a collaboration designed to generate high-quality genomic

data on up to 50 types of cancer over the next decade.

"Cancer's complexity poses an enormous challenge. NIH is highly encouraged that the worldwide scientific community is joining to meet this challenge, and we are pleased to be a member of this ambitious international endeavor," said NIH Director Elias Zerhouni. "The consortium's commitment to making its data rapidly available in public databases will serve to accelerate research into the causes and control of cancer in the United States and throughout the world."

Each ICGC member intends to conduct a comprehensive, high-resolution analysis of the full range of genomic changes in at least one specific type or subtype of cancer, with studies built around common standards of data collection and analysis. Each project is expected to involve specimens from approximately 500 patients and have an estimated cost of $20 million.

As part of its coordination efforts, the ICGC will generate a list of approximately 50 cancer types and subtypes that are of clinical significance around the globe. ICGC members plan to assume responsibility for specific cancers, and one of the ICGC's roles should be to facilitate the exchange of information so participants' efforts do not duplicate each other.

TCGA Pilot To Become Part of Consortium

The NIH contribution to the ICGC will be The Cancer Genome Atlas pilot project, which is jointly funded by NCI and the National Human Genome Research Institute for a total of $100 million.

NIH isn't contributing any additional funds to the ICGC, a spokesman said.

Besides NIH, current ICGC members include:

—Australia: National Health and Medical Research Council (Observer Status)

—Canada: Genome Canada (Observer Status); Ontario Institute for Cancer Research

—China: Chinese Cancer Genome Consortium

—Europe: European Commission (Observer Status)

—France: Institut National du Cancer

—India: Department of Biotechnology, Ministry of Science & Technology

—Japan: RIKEN; National Cancer Center

—Singapore: Genome Institute of Singapore

—United Kingdom: The Wellcome Trust; Wellcome Trust Sanger Institute

"Clearly, there is an urgent need to reduce cancer's terrible toll. To help meet that need, the consortium will use new genome analysis technologies to produce comprehensive catalogs of the genetic mutations involved in the world's major types of cancer," said Thomas Hudson, of the ICGC Secretariat, which is based at the Ontario Institute for Cancer Research in Toronto. "Such catalogs will be valuable resources for all researchers working to develop new and better ways of diagnosing, treating and preventing cancer."

Worldwide, more than 7.5 million people died of cancer and more than 12 million new cases of cancer were diagnosed in 2007. Those numbers are expected to rise to 17.5 million deaths and 27 million new cases in 2050.

The ICGC's main criteria for prioritizing cancer types include: impact, including incidence and mortality rates, availability of therapies and age of onset; scientific interest; and feasibility, which includes the ability to obtain enough high-quality samples to conduct a large-scale project.

To facilitate comparisons among different types of cancer, the ICGC guidelines list key factors for its members to consider in the production of genomic catalogs. Those factors include comprehensiveness, which involves detecting all cancer-related genetic mutations that occur in at least 3 percent of tumor samples; resolution, which involves generating data at the level of individual DNA bases; quality, which involves monitoring based on common standards for pathology and technology; and controls, which involves comparisons of data from matched, non-tumor tissue.

ICGC member nations plan to agree to common standards for informed consent and ethical oversight. While the informed consent process will necessarily differ according to each member country's requirements, the consortium's policies state that cancer patients enrolled in an ICGC-related study should be informed that their participation is voluntary, that their clinical care will not be affected by their participation and that data obtained from analyses using their samples will be made available to the international research community. ICGC members also should take steps to ensure that all samples will be coded and stored in ways that protect the identities of the participants in the study.

Data from ICGC member research will be made rapidly available to qualified investigators. Consortium participants intend not to file any patent applications or make other intellectual property claims on primary data from ICGC projects.

The ICGC is open to all entities that accept its policies and guidelines.

A white paper detailing those policies and guidelines is available on the consortium's Web site at www.icgc.org.

In the Cancer Centers:

M.D. Anderson, German Center Sign Research Agreement

(Continued from page 1)

. . . **M. D. ANDERSON** Cancer Center signed a sister institution agreement with the German Cancer Research Center of Heidelberg. The agreement formalizes long-standing academic relationships among faculty at both institutions, and solidifies plans to collaborate in cancer research. The signing ceremony, which took place in Heidelberg, included **John Mendelsohn**, president of M. D. Anderson Cancer Center, and **Otmar Wiestler**, chairman and scientific director of the German Cancer Research Center. "The synergy of our respective programs presents considerable opportunities to further accelerate the process of bringing promising cancer therapies from the laboratory bench to the patient's bedside," said Mendelsohn. The agreement originates from relationships between faculty and scientists at both institution, which date back 15 years in the areas of radiation oncology, neuro-oncology, immunotherapy and blood cancer, among others. A more formal approach to academic collaboration was advanced in 2006, when a delegation of scientists and administrators from the German Cancer Research Center, led by Wiestler, visited M. D. Anderson to discuss areas for specific collaborative projects, training exchanges for junior scientists, and a longer–term relationship between the two institutions. The signing ceremony and workshop was attended by nine M. D. Anderson faculty members including **Radhe Mohan**, chairman of the Department of Radiation Physics; **Uwe Titt**, assistant professor in the Department of Radiation Physics; **John Hazle**, chairman of the Department of Imaging Physics; **Edward Jackson**, professor in the Department of Imaging Physics; **Georg Halder**, associate professor in the Department of Biochemistry and Molecular Biology; **Gordon Mills**, chairman of the Department of Systems Biology; **W. K. Alfred Yung**, chairman of the Department of Neuro-Oncology; **Kenneth Aldape**, professor in the Department of Pathology and **Hilario Mata**, project director of Extramural Programs. . . . **ROSWELL PARK** Cancer Institute appointed **Camille Wicher** vice president of corporate ethics and research subject protection. She will advise scientists, clinicians and the administration on ethical practices and scientific integrity within all facets of the institute. She also will be chairman of the corporate ethics and clinical ethics committee and the institutional conflicts of interest committee. Wicher joined RPCI in 1997 as counsel for risk management and corporate compliance and was named assistant vice president for research subject protection and scientific integrity in 2002. . . . **MEMORIAL SLOAN-KETERRING** Cancer Center named **Kathy Lewis** vice president of public affairs. She will oversee communication efforts including media relations, website design and content, publications, community affairs, and special events. From 2004 to 2007, Lewis was president and CEO of the Christopher and Dana Reeve Foundation. Lewis succeeds **Anne Thomas**, who retired last fall. . . . **EMORY WINSHIP** Cancer Institute is offering a support program for children ages six to 11 whose parents have been diagnosed with cancer. "The program focuses on the children, and how they can express their feelings and learn more about what a cancer diagnosis means," said **Rebecca Sizemore**, social worker at Emory Winship and director of the program, called Children's Lives Include Moments of Bravery. The next CLIMB program begins June 3, and will run for six weeks.

Funding Opportunities:

RFA-CA-08-015: Community Clinical Oncology Program. U10. 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-08-015.html. Inquiries: Lori Minasian, 301-496-8541; minasilo@mail.nih.gov.

RFA-CA-08-016: Minority-Based Community Clinical Oncology Program. U10. June 10; Application Receipt Date: July 10. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-08-016.html. Inquiries: Worta McCaskill-Stevens, 301-496-8541; mccaskiw@mail.nih.gov.

PA-08-161: Transdisciplinary Research on Fatigue and Fatigability in Aging. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-08-161.html. Inquiries: Ann O'Mara, 301-496-8541; omaraa@mail.nih.gov.

PA-08-162: Transdisciplinary Research on Fatigue and Fatigability in Aging. R21. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-08-162.html.

RFP N02-PC-85002-29: Development of the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events. Full text: http://www.fbodaily.com/archive/2008/04-April/05-Apr-2008/FBO-01547039.htm. Inquiries: Elizabeth Dean, deane@mail.nih.gov.

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THE CANCER LETTER

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Business & Regulatory Report

Product Approvals & Applications:

Antigenics' Oncophage Registered In Russia For Kidney Cancer Treatment

Antigenics Inc. (NASDAQ:AGEN) said the Russian Ministry of Public Health has issued a registration certificate for Oncophage (vitespen) in kidney cancer with intermediate risk for disease recurrence.

"The standard of care for nonmetastatic renal cell carcinoma is surgical removal of the kidney followed by observation," Vsevolod Matveev of N.N. Blokhin's National Cancer Research Center of RAMS, Moscow, said in a statement. "Following surgery, patients often request treatment options to

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Deals & Collaborations:

Roche To Buy Piramed For P13-K Inhibitors In Oncology, Other Diseases

Roche of Nutley, N.J., said it would acquire **Piramed Ltd**., of the U.K., gaining access to the Piramed research programs targeting PI3-K-alpha in oncology and PI3-K-delta in inflammatory disease.

Under the agreement, Roche said it would acquire 100 percent of the Piramed shares for $160 million, plus a milestone payment of $15 million, which is due upon the commencement of phase II trials for the company oncology program.

The PI3-K pathway plays a role in disease progression and in resistance to chemotherapeutics in cancer cells, the company said. Pre-clinical studies have demonstrated the activity of PI3-K inhibitors in tumors such as breast and lung cancer, as well as inflammatory diseases such as rheumatoid arthritis.

Caliper Life Sciences Inc. (NASDAQ:CALP) of Hopkinton, Mass., said it has formed a partnership with **Horizon Discovery Ltd.**, of Cambridge, U.K., to use isogenic cell lines to screen for targeted cancer drugs using genetically defined in-vitro disease models.

Through the alliance, CDAS said it now has genetically-defined, and isogenic human cancer cell lines that can identify and characterize personalized drugs targeted at a specific subset of patients.

"The addition of the Horizon isogenic cell lines to our oncology cell proliferation panel, and the ability to correlate results from the isogenic cell lines to efficacy in specific patient populations, further solidifies the Caliper in vitro-in vivo-human bridge," said David Manyak, executive vice president of drug discovery services, Caliper Life Sciences. "Access to the

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Oncophage Registered In Russia For Kidney Cancer

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help prevent or delay recurrence. This registration means patients in Russia with earlier-stage disease will now have Oncophage as a treatment option."

To comply with U.S. regulations for exporting biologics, Antigenics said it applied for an export license from FDA.

Russian Ministry of Public Health registration was based on the largest, randomized, phase III kidney cancer trial ever completed in the adjuvant treatment setting, the company said. In the study, 604 eligible patients who were without renal cell carcinoma disease at baseline were randomized at 118 centers worldwide, including 172 patients (28 percent) at eight sites in Russia. The primary efficacy data are being prepared for scientific publication, the company said.

Findings from investigator-reported data showed that treatment with the agent in the intermediate-risk population (stages I/II high-grade, III T1/2/3a low-grade without disease at baseline (n = 362) demonstrated a clinically significant improvement in recurrence-free survival of approximately 45 percent over the observation arm ($P < 0.01$; hazard ratio = 0.55), the company said. Although the median has not yet been reached, results from the 25th percentile indicate that recurrence-free survival was extended by about 1.7 years.

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Adverse events were constitutional in nature or related to the actual injection, and included, but were not limited to, injection site erythema, injection site induration, injection site pain, injection site edema, headache, fatigue and rash, the company said.

Derived from the tumor of the individual, Oncophage contains the antigenic fingerprint of the cancer, the company said. The agent then reprograms the immune system to target only cancer cells bearing the fingerprint, the company said.

BioVex Inc. of Woburn, Mass., said FDA approved the design of a single phase III trial OncoVEX (GM-CSF) in treated metastatic melanoma under the Special Protocol Assessment procedure.

BioVex said it is concluding a 50-patient phase II trial for the drug stand alone therapy in unresectable stage IIIc and stage IV metastatic melanoma. The trial measured overall objective response, which is defined as a complete response, or partial response, where there is a >30 percent reduction in disease burden. Interim results demonstrated an encouraging rate of durable objective response with multiple patients with metastatic disease at enrollment having been declared disease free following therapy, the company said.

The phase III study will also enroll treated unresectable stage IIIc and stage IV disease using OncoVEX as monotherapy, the company said. The primary efficacy endpoint also will be response rate-based; the primary objective being to demonstrate a statistically significant increase in the rate of objective responses maintained for six months or more, in comparison to control therapy, or subcutaneously administered GM-CSF. The study would enroll 360 evaluable patients randomized such that 240 patients receive OncoVEXand 120 receive control, the company said.

OncoVEX is an unpartnered, first-in-class oncolytic, which works by 1) replicating and spreading within solid tumors, causing the death of cancer cells; while 2) stimulating the immune system to destroy metastatic deposits.

Cephalon Inc. (NASDAQ:CEPH) of Frazer, Pa., said the European Commission granted marketing authorization for Effentora, a buccal tablet formulation of fentanyl for breakthrough cancer pain in adults receiving maintenance opioid therapy for chronic pain.

The approval allows Cephalon to market Effentora in the 27 member states of the E.U., as well as Iceland and Norway, the company said.

Effentora utilizes the proprietary OraVescent drug delivery technology to permit absorption of the opioid fentanyl across the inner lining of the cheek at a rate designed to match the onset of a breakthrough pain episode. The safety and efficacy of the product were evaluated in two double-blind, randomized, placebo-controlled crossover studies of 248 cancer patients with breakthrough pain who experienced between one and four episodes of breakthrough pain per day and who were already taking maintenance opioid therapy, the company said. An extension study has demonstrated safety and tolerability in 197 patients followed over a six-month period.

Favrille Inc. (NASDAQ:FVRL) of San Diego said it is developing patient-specific, active immunotherapies for cancer and it has reached the data cutoff date for the phase III registration trial of Specifid (mitumprotimut-T, formerly FavId) following Rituxan in follicular B-cell non-Hodgkin's lymphoma.

As of the data cutoff date, 205 of the 349 patients randomized have experienced disease progression according to investigator determination, the company said. Final analysis would be based on a central radiology assessment of the CT scans. Unblinding of the data would occur in June.

Median follow-up for ongoing patients is 31 months from randomization (range 21 to 41 months), or 34 months from the initiation of Rituxan treatment (range 24 to 44 months). Based on the assumptions of the protocol, the range of follow-up would detect a significant difference between the two arms for time to progression, the primary endpoint, the company said.

Initiated in July 2004, the trial was open to both treatment-naive and previously treated patients, ultimately enrolling a much larger treatment-naive population (78 percent). Randomization was done at a one-to-one ratio to receive either Specifid or placebo following a standard course of Rituxan. A total of 45 patients came off study and were permanently censored for reasons other than disease progression, 28 (8 percent) because Specifid was not produced and 17 (5 percent) for a variety of other reasons.

In October 2007 an independent Data Monitoring Board conducted an administrative analysis of the unblinded control arm, the company said. The objective of the analysis, conducted in agreement with FDA, was to assess the behavior of disease progression in the control arm to determine the duration of follow-up needed prior to unblinding the trial.

The outcome of this DMB analysis supported the rationale for the timing of data cutoff.

Specifid is based upon a recombinant protein, called idiotype, which is derived from genetic material obtained from the tumor, then conjugated to keyhole limpet hemocyanin, a protein that boosts immune responses.

GammaStar Medical Group Ltd. of Shanghai said it received the CE certification for E.U. medical devices for its Gyro Knife, a kind of radiotherapy equipment.

Insmed Inc. (NASDAQ:INSM) of Richmond said it has received approval from the U.K. Medicines and Healthcare products Regulatory Agency to initiate a clinical study of INS-19, its follow-on biologic product candidate.

The agent, which is a recombinant form of human G-CSF, is a follow-on biologic of the FDA-approved product Neupogen, which had U.S. sales of $0.9 billion in 2007, the company said.

Pre-clinical studies demonstrate that INS-19 and FDA-approved Neupogen are comparable in both their pharmacological and toxicological profile, the company said. Detailed analytical characterization also demonstrates that the products have a high degree of similarity.

The phase I study would be conducted in the U.K. and would compare the safety and establish the bioequivalence of INS-19 to Neupogen, the company said. The trial is the first of two planned for 2008 as part of the Insmed development of a portfolio of FOBs, the company said. The patent covering Neupogen expires in 2013.

Recombinant human G-CSF is a synthetic version of a human G-CSF that is produced in bacteria, the company said. The G-CSF mimics the biological effects of naturally occurring G-CSF and is used to treat medical conditions including neutropenia in cancer, bone marrow transplantation, or in chronically low neutrophils for other reasons.

Medarex Inc. (NASDAQ:MEDX) and **Bristol-Myers Squibb Co.** (NYSE:BMY) said they will delay the Biologics License Application submission for ipilimumab, an investigational immunotherapy for advanced metastatic melanoma, after meeting with FDA.

The agency has requested additional overall survival data to demonstrate the benefit of the immunotherapy, the companies said.

The randomized phase III trial evaluating the efficacy of ipilimumab in combination with dacarbazine versus dacarbazine alone in untreated unresectable stage III or stage IV melanoma is ongoing under Special Protocol Assessment. The companies said they are in discussions with FDA to change the primary endpoint from progression free survival to OS. A submission for melanoma would include survival data from the phase II second-line studies and the randomized ongoing phase III first-line trial.

The companies also said they have ongoing phase II studies in hormone-refractory prostate cancer and lung cancer as well as a phase III study, to be initiated, in adjuvant melanoma.

Ipilimumab is being developed through a partnership between Bristol-Myers Squibb and Medarex.

Morphotek Inc. of Exton, Pa., said the European Commission has granted Orphan Drug status to the monoclonal antibodies farletuzumab (MORAb-003) for ovarian cancer and MORAb-009 for pancreatic cancer.

Farletuzumab is in a phase II efficacy study for platinum sensitive ovarian cancer, the company said. In phase I studies, the agent was well tolerated in advanced, platinum-resistant or refractory ovarian cancer over the course of the treatment period and clinical observations suggested pharmacological activity, the company said.

MORAb-009 is in a phase II study in first-line therapy with gemcitabine for inoperable pancreatic cancer. The agent was well tolerated in phase I studies and clinical observations from the studies suggested anti-tumor activity, the company said.

"The phase I study results for each molecule were promising, and the ongoing phase II studies would evaluate their efficacy in combination with accepted chemotherapy regimens in ovarian or pancreatic cancer," said Martin Phillips, senior vice president of clinical development for Morphotek.

The studies are being conducted in Europe, the U.S., Argentina and Brazil.

Theranostics Health of Rockville, Md., said it has received an exclusive license from NIH to commercialize microdissection including Laser Capture Microdissection combined with protein analysis for cancer diagnostics and companion diagnostics.

Under the agreement, Theranostics Health would pay NIH the customary license issue royalties, minimum annual royalties, benchmark and earned royalties upon commercialization of the technology, the company said.

"Existing methods of genomic and proteomic tissue profiling analysis that do not rely on LCM have been shown to produce inaccurate and possibly misleading results, arising from heterogeneity of tissues and variation in cellular compositions between samples and within different regions of a tissue sample," said Lance Liotta, co-inventor of the technology, co-founder and chief medical officer, Theranostics Health. "This licensed technology allows us to precisely collect and analyze the specific cells of interest from patient samples."

"But this is only the first step," said Emanuel Petricoin, co-inventor of the technology, co-founder and chief scientific officer of Theranostics Health. "Our unique signaling pathway profiling platform allows the activity of theranostic biomarkers of interest to be quantitatively measured from microdissected patient samples. With the technology and our experience and expertise in disease signaling pathways, we are more effectively treating patients with existing drugs and treating patients who are resistant to their therapies."

Deals & Collaborations:

Indevus, Orion In Agreement On Marketing Vantas Implant

(Continued from page 1)

tools would enhance the success rate and reduce the cost of discovering targeted monotherapy or combination therapies that better treat disease with fewer adverse events."

Indevus Pharmaceuticals Inc. (NASDAQ: IDEV) of Lexington, Mass., said it has signed a license, supply and distribution agreement with **Orion Corp.** granting Orion the rights to market Vantas (histrelin acetate subcutaneous implant) in Europe as well as other countries.

Vantas is a 12-month implant for advanced prostate cancer, which is undergoing the mutual recognition procedure for further European approvals, the company said.

The Vantas implant utilizes the Indevus patented Hydron polymer technology, the company said.

Under the agreement, Orion would pay a $7 million up-front payment and various contingent payments related to approvals and sales thresholds, which total $14 million, the company said. Additionally, Indevus said it has agreed to supply the product to Orion at a pre-

determined transfer price subject to annual minimum purchase requirements beginning next year.

Vantas is a soft and flexible 12-month hydrogel implant that provides histrelin, a luteinizing hormone-releasing hormone agonist, for advanced prostate cancer. The implant is contraindicated in hypersensitivity to GnRH, GnRH agonist analogs, or any components in Vantas, the company said.

Intradigm Corp. of Palo Alto said it has licensed intellectual property covering efficacy-enhancing structural elements of small interfering RNA from the **University of Massachusetts Medical School**.

The licensed IP includes parameters for the structural modifications for next generation siRNAs including the Zamore Design Rules that improve RNAi therapeutics, the company said. The technology allows Intradigm to incorporate siRNA sequences into its proprietary RNAi delivery systems.

"Because the RNAi research being conducted in our labs may bring RNAi therapeutics to patients who desperately need them, we are driven to align with leaders in the RNAi therapeutic space, such as Intradigm, to provide them access to our intellectual property and support their important drug development efforts," said James McNamara, executive director of the Office of Technology Management at the University of Massachusetts Medical School.

The RNAi NPX delivery technology is a modular, multi-component delivery vector that carries active siRNA molecules in its core with the flexibility to attach a Polyethylene Glycol layer and/or a targeting ligand to the polymer-siRNA NPX to improve circulation half life and achieve selective distribution to the target tissue, the company said. At the core of the RNAi NPX delivery technology is known as PolyTran. PolyTran, the Intradigm proprietary peptide-based biodegradable polymer, enables systemic delivery of the siRNAs. Additionally, the platform offers tissue specific targeting of siRNA through the attachment of specific ligands directed to target cell receptors, the company said.

Leukemia & Lymphoma Society of White Plains, N.Y., said it has entered into a $2.9 million, three-year collaborative research arrangement funded through the LLS Therapy Acceleration Program with **Anjin Group Inc.** to develop a fusion toxin protein for acute myelogenous leukemia.

The TAP program advances therapies with high prospects of providing near-term benefit for blood cancers, the society said.

"Our partnership with Anjin Group, the largest announced to date under LLS Therapy Acceleration Program, is the result of a detailed, year-long selection process," said Louis DeGennaro, chief scientific officer of LLS. "As a results-oriented, patient-focused company with a genuine interest in hematological cancers, Anjin Group aligns very well with the goals of TAP."

Lorus Therapeutics Inc. (TSX: LOR; AMEX: LRP) of Toronto said its subsidiary **GeneSense Technologies Inc.** has signed an exclusive multinational license agreement with **Zor Pharmaceuticals LLC**, a subsidiary of Zoticon Bioventures Inc., to develop and commercialize Virulizin for therapeutic applications.

The initial clinical development would be for advanced pancreatic cancer, the company said.

Under the terms of the agreement, GeneSense said it would receive payments of $10 million upon achievement of milestone events and royalties from 10-20 percent depending on sales of Virulizin and subject to other adjustments. In addition, a wholly owned subsidiary of Lorus, Pharma Immune Inc., would receive 25 percent of the initial equity in Zor Pharmaceuticals. The Pharma Immune equity would not be subject to dilution on the first $5 million of financing in Zor Pharmaceuticals. Thereafter, Pharma Immune could participate in any additional financings to maintain its ownership level. In addition, GeneSense said it has entered into a service agreement with Zor Pharmaceuticals to transfer knowledge and establish a foundation for the development program for Virulizin.

Zor Pharmaceuticals would be responsible for clinical development, regulatory submissions and commercialization of the product in North and South America and Europe, the company said. GeneSense would retain rights in other countries, including Japan, Australia and New Zealand.

Virulizin is a biological response modifier or immunotherapeutic agent that stimulates the immune system through different mechanisms, including the activation of macrophages and the infiltration of natural killer cells into tumors, the company said. The agent has demonstrated high levels of antitumor activity in cancer indications including pancreatic cancer.

Medicsight PLC subsidiary of **MGT Capital Investments Inc.** (AMEX:MGT) said it has entered into a global partnership with **INFINITT** for colorectal cancer detection.

Combined INFINITT-Medicsight products for colorectal cancer detection would be distributed using

the INFINITT global network of offices in six countries and partners and sales channel representatives in 20 other countries, the company said.

The Medicsight ColonCAD software would be integrated into the INFINITT PACS and 3D Rapidia Virtual Colonoscopy workstations, the company said. The latter is a next- generation colorectal cancer screening tool.

"CT Colonography for the screening of colorectal cancer is now at the forefront of screening technologies, " said Se Hyung Kim, assistant professor, Department of Radiology, Seoul National University. "Partnerships such as that between Medicsight and INFINITT which deliver cutting edge 3D and CAD technologies to radiologists around the world are vital to increase the adoption of this very important and life saving technique."

Parkway Health said three hospitals that it operates in Singapore have become the first medical institutions to join **Companion Global Healthcare Inc.,** of South Carolina, a U.S.-based health care network, giving American patients access to health care at pre-negotiated, in-network rates that are lower than rates at U.S. hospitals.

Access to the three Singapore hospitals is now available to the members of BlueCross Blue Shield of South Carolina and BlueChoice HealthPlan of South Carolina through the Companion Global Healthcare network at preferred rates, ParkwayHealth said. Companion Global Healthcare also serves the uninsured, and is available to contract with insurance companies and employer groups that wish to include an overseas option in their benefit plans.

A range of medical and surgical services is available, including joint replacements, open heart and cardiology surgery, and invasive cancer treatment, Parkway said.

Each hospital is accredited by the Joint Commission International, the affiliate of The Joint Commission, the largest accreditor of health care organizations in the U.S., said ParkwayHealth.

Poniard Pharmaceuticals Inc. (NASDAQ: PARD) of South San Francisco said it has selected the **AltheaDx Inc.** Express Pathway program to identify molecular signatures, which may be correlated to platinum resistance.

Picoplatin, the Poniard lead product candidate, is a new generation platinum agent that overcomes platinum resistance, the company said. The development of molecular signatures of platinum resistance could predict clinical response to picoplatin treatment and may improve outcomes in platinum-resistant cancers.

Clinical trials of intravenous picoplatin include a phase III trial in small cell lung cancer and phase II trials in metastatic colorectal and hormone-refractory prostate cancers, as well as a phase I trial of oral picoplatin in solid tumors, the company said.

Raven Biotechnologies Inc. of South San Francisco said it has entered into an agreement with **Monogram Biosciences Inc**., under which Monogram would evaluate Raven monoclonal antibodies for use with its VeraTag technology in diagnosing cancer.

"Through our collaboration with Monogram we hope to accelerate the development of targeted oncology therapeutics," said George Schreiner, CEO of Raven biotechnologies.

The Raven technology platform has generated well-characterized, high-affinity monoclonal antibodies to proteins on the cell surface that can identify and validate targets, the company said. The platform has delivered a library of antibodies targeting new and recognized antigens. Raven said it is focusing on antibody-based therapeutics targeting lung, colon, pancreatic, prostate, breast, and ovarian cancer.

RAV12, the lead Raven product candidate, targets adenocarcinomas and is in clinical development for gastrointestinal and other cancers, the company said. The discovery process simultaneously identifies cell-surface drug targets and the antibody therapeutics to regulate them.

Rosetta Genomics Ltd. (NASDAQ:ROSG) of Rehovot, Israel, said it has signed an agreement with **University of California, Irvine School of Medicine** for diagnostic tests based on the Rosetta microRNA technology. The tests differentiate squamous versus non-squamous lung cancer, differentiate mesothelioma from adenocarcinoma, and identify cancers of unknown primary origin, the company said.

"There is a large body of research into the significant potential microRNAs hold as powerful biomarkers, and we are excited to develop and validate assays using the Rosetta Genomics microRNA technology," said John Krolewski, of the University of California, Irvine.

TopoTarget A/S (OMX: TOPO) of Copenhagen said it now wholly owns global rights to belinostat, its lead product in clinical development.

Under the agreement, CuraGen has agreed to sell the rights to belinostat back to TopoTarget and will

receive $26 million, the company said. CuraGen also would receive 5 million new TopoTarget shares issued through a directed issue of shares, and a commercial milestone payment of $6 million, which is defined as 10 percent of the first $60 million of belinostat sales or partnership revenues, the company said.

The agent has shown positive results including proof of concept in Cutaneous and Peripheral T-Cell Lymphoma as well as ovarian cancer in combination with standard chemotherapy drugs, the company said.

The product has been developed for multiple cancer indications jointly by TopoTarget and CuraGen Corp. since 2004.

"CuraGen has been a good partner and helped us over a high risk period," said Peter Jensen, CEO of TopoTarget. "More than 500 patients have been treated with the agent, and we are enthusiastic about its efficacy and safety. The drug is broadly applicable and unique in its flexible dosing, and its lack of toxicity."

Belinostat is a small molecule HDAC inhibitor in 18 clinical trials, 10 of which are sponsored by NCI for different cancers, the company said. The drug can be administered both intravenously and orally in capsule form.

University of North Carolina at Chapel Hill and **Hamner Institutes for Health Sciences** of Research Triangle Park, N.C., said they have signed a memorandum of understanding to collaborate in basic and translational research.

The partnership was established with the North Carolina schools of medicine, pharmacy and public health, and its Kenan-Flagler Business School to advance human therapeutics and public health locally and internationally.

Initial areas of collaboration include therapies for cancer and respiratory diseases by advancing experimental and computational sciences in drug safety assessment, drug disposition, pharmacogenomics, genomic medicine, nanomedicine, drug delivery and public health.

The scientific and business-development teams at Hamner Institutes will work with UNC faculty, including from the Center for Integrative Chemical Biology and Drug Discovery in the Schools of Pharmacy, Medicine and College of Arts and Sciences, UNC Kenan-Flagler Business School and the University Office of Technology Development to identify, assess and enhance development of research leads. The partners would pursue research grant opportunities from government, industry and non-profit organizations for research and technologies development that can be licensed out and/or spun out into the new innovation center of the university.

The partnership will draw on resources at other academic institutions in the state and the North Carolina Biotechnology Center, which supports statewide faculty recruitment, scientific education, economic development and technology development.

Xceed Molecular of Wellesley, Mass., said the **University of Florida** has joined the Xceed Strategic Collaborator program to develop a molecular test for early-stage bladder cancer.

Xceed said it would work with primary researchers, Charles Rosser, Department of Urology, and Steve Goodison, Department of Surgery, University of Florida, to perform verification and validation of an expression signature to differentiate bladder cancer from other conditions using voided urine samples.

As part of the collaboration, Xceed and UF said they would test 700 samples of either cancerous or non-cancerous bladder tumors to verify that the expression signature is useful in distinguishing the two populations. Xceed would run the first 100 samples on its Ziplex System in its expression-services laboratories in Toronto to optimize the performance of the signature on the Ziplex platform. Xceed would also supply the university with the Ziplex System to study the remaining samples.

Clinical Trials:

CuraGen Drug In Phase II Trial For Unresectable Melanoma

CuraGen Corp. (NASDAQ:CRGN) of Branford, Conn., said it has advanced its antibody-drug conjugate, CR011-vcMMAE, into a phase II trial for unresectable stage III and stage IV melanoma.

CR011-vcMMAE is an ADC comprised of a fully-human monoclonal antibody against glycoprotein NMB attached to a synthetic drug monomethyl auristatin E, using the **Seattle Genetics** proprietary technology.

Delcath Systems Inc. (NASDAQ:DCTH) said the Institutional Review Board of the University of Maryland Medical Center approved the UMMC participation in the phase III study of the Delcath Percutaneous Hepatic Perfusion System for the isolated, high dose delivery of the anti-cancer agent melphalan for inoperable metastatic melanoma in the liver.

The study is being led by NCI, which approved the

expansion of the study to a multi-center trial.

UMMC also entered into a clinical research agreement with Delcath enabling the hospital to recruit and treat patients, the company said.

"The Delcath System may represent an effective, minimally toxic means of restoring liver health and improving patient outcome, said Richard Alexander, professor of surgery and chief of urology at the University of Maryland and principle investigator.

Alexander was deputy director of the NCI Center for Cancer Research, and principal investigator of the phase I study that was fast-tracked to the phase III study.

The Delcath System delivers higher doses of anti-cancer drugs to the liver while preventing entry of the drugs to the rest of the circulation. This isolation limits toxicities that result from systemic chemotherapy treatments, the company said.

In the trial, randomization would be into one of two treatment arms, including immediate treatment with melphalan via the Delcath System or treatment with best alternative care, the company said. The study would evaluate the duration of tumor response in each of the two study arms. Following guidelines established by FDA under a Special Protocol Assessment, when disease progresses in the best alternative care arm of the trial, patients are permitted to cross over and receive treatment with the Delcath System, the company said.

EntreMed Inc. (NASDAQ:ENMD) Rockville, Md., said it has begun a phase I, dose-escalation study for its selective kinase inhibitor, ENMD-2076, in advanced cancer.

Wells Messersmith, of the University of Colorado Cancer Center, co-principal investigator.

ENMD-2076, which inhibits angiogenesis, has demonstrated substantial, dose-dependent efficacy as a single agent in multiple preclinical models, including tumor regression in breast, colon, and leukemia models, the company said. The oral agent that has shown an acceptable toxicity profile in preclinical studies without cardiovascular toxicity.

The trial would assess safety and tolerability of the product in refractory cancer, the company said. Pharmacokinetics would be assessed to determine a dose-dependent response.

Epeius Biotechnologies Corp. of San Marino, Calif., said interim analysis of a phase I/II study of Rexin-G for pancreatic cancer confirmed anti-tumor activity with no major toxicity in metastatic chemotherapy-resistant pancreatic cancer.

The trial design includes five escalating doses of intravenous Rexin-G ranging from 1 x 10e11 cfu twice a week to 4 x 10e11 cfu three times a week for four weeks, the company said. Treatment cycles are repeated if grade 1 or less toxicity is exhibited. Interim analysis showed no dose limiting toxicities in nine evaluable patients who received dose levels 1-3. Furthermore, the analysis showed decrease in tumor size or disease stabilization (by RECIST), decreased metabolic activity in tumors (by PET-CT scan), reduction in tumor marker levels, and clinical benefit with dose level 3. The second phase of the study has now opened with six patients receiving dose levels 4 and 5, respectively, as the adaptive study design evaluates the over-all safety for the optimal dosing regimen in a phase II/III trial, the company said.

Sant Chawla, principal investigator of the phase I/II study, also is conducting three Los Angeles-based phase I/II trials using the agent in sarcoma, pancreatic cancer, and breast cancer, and a phase II study of Rexin-G for osteosarcoma.

Rexin-G is a targeted injectable genetic medicine whose nanoparticles destroy both primary tumors and metastatic cancers, the company said.

Kosan Biosciences Inc. (NASDAQ:KOSN) of Hayward, Calif., said it has begun a phase II trial of epothilone KOS-1584 for non-small cell lung cancer.

The trial is an open-label, multi-center, monotherapy study for measurable advanced or metastatic non-small cell lung cancer with only one prior chemotherapy regimen, the company said. The primary endpoint is objective response rate. Secondary endpoints include progression-free survival, time to progression, time to treatment failure, time to response, duration of response and overall survival.

KOS-1584 would be administered via a 3-hour intravenous infusion weekly for two weeks out of every three weeks at a dose of 25 mg/m.

The trial would enroll up to 50 patients in a two-stage Simon design, the company said.

KOS-1584 is a member of a class of cytotoxic macrolides capable of causing mitotic arrest by polymerization of cellular microtubules, the company said. The agent has demonstrated antitumor activity and favorable tolerability in phase I trials for solid tumors, including tumor shrinkage measured by objective responses in non-small cell lung, ovarian and pancreatic cancers, as well as durable stable disease in additional tumors, the company said.