THE CANCER LETTER

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Von Eschenbach Candidacy For FDA Hampered By Three Republican Holds

By Paul Goldberg

Andrew von Eschenbach's chances of being confirmed as FDA commissioner during the lame duck session of Congress have vanished as another Senator put a hold on his nomination.

Sen. Charles Grassley (R-Iowa) said he objected to von Eschenbach's candidacy, citing the acting commissioner's failure to comply with his subpoenas.

"The actions and words of this nominee display a misunderstanding of congressional oversight of the executive branch of government," Grassley said in a statement Nov. 30. "The nominee is not well-served by advisers who say that executive agency policy somehow trumps the Constitution."

Grassley took the third place in a line of Republicans who said they

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In the Cancer Centers:

Meharry, Vanderbilt Win $14M Renewal; Indiana Cancer Center Receives $50M Gift

MEHARRY/VANDERBILT-INGRAM Cancer Partnership was awarded $14 million by NCI to reduce cancer mortality among African Americans and other minorities. The renewal grant will provide $10 million to Meharry Medical College and $4 million to Vanderbilt-Ingram Cancer Center. **Harold Moses**, professor and director emeritus of the cancer center, is the principal investigator. Meharry also will collaborate with Tennessee State University to develop community outreach and prevention strategies to strengthen community center cancer education, behavioral modifications, and interventions, said **Samuel Evans Adunyah**, professor and chairman of Cancer Biology Division at Meharry. . . . **INDIANA UNIVERSITY** Cancer Center received a $50 million gift from philanthropists **Melvin** and **Bren Simon**. The cancer center research program and patient-care facilities will be named the Indiana University Melvin and Bren Simon Cancer Center. Half of the gift will be used to create the Joshua Max Simon Research Endowment to recruit and retain researchers to the Indiana University School of Medicine and to support the laboratory research programs at the cancer center. The other half will fund the expansion of the cancer center patient-care facility, a collaboration between the Indiana University School of Medicine and Clarian Health. . . . **CITY OF HOPE** announced seven staff appointments within the Beckman Research Institute, as part of a multi-year effort to recruit more than

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Resistance To Subpoenas Triggers Grassley's Hold

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would block von Eschenbach. Sen. Jim DeMint (R-SC) put a hold on the candidacy to protest the availability of the abortion drug RU-486, and Sen. David Vitter (R-La.) lodged an objection pending legalization of importation of prescription drugs.

Across the aisle, Senators Hillary Rodham Clinton of New York and Patty Murray of Washington were the first to object to von Eschenbach's candidacy, but dropped their hold on the nomination after FDA approved the Plan B emergency contraceptive last summer. Sen. Dianne Feinstein (D-Calif.), von Eschenbach's long-time ally in cancer politics, recently issued a statement slamming FDA for approving silicone gel breast implants, but stopped short of putting yet another hold.

Grassley holds von Eschenbach personally responsible for the agency's insufficient cooperation with his investigation of the handling of the antibiotic Ketek (telithromycin), sponsored by SanifiAventis.

"As chairman of the Finance Committee, I am extremely disturbed by the Acting Commissioner's failure to comply with the committee's subpoenas over the past six months," Grassley wrote in a Nov. 16 letter to Senate Majority Leader Bill Frist (R-Tenn.)

Von Eschenbach wasn't at FDA during the years when Ketek was going through the approval process. However, after coming to the agency as acting commissioner in 2005, he has become part of a controversy that features scientific fraud, deadly toxicities, and allegations of lax regulatory oversight, critics says.

In earlier correspondence with the agency, Grassley alleged that in the case of Ketek, von Eschenbach intimidated whistleblowers at the agency and became involved in efforts to resist his subpoenas.

In the letter to Frist earlier this month, Grassley also noted that he and Sen. Max Baucus (D-Mont.) had met with HHS Secretary Mike Leavitt to protest the department's failure to comply with the subpoenas and to "let him know, in no uncertain terms, that failure to comply with the committee subpoenas was unacceptable," the letter states.

"We also advised Secretary Leavitt that numerous other committee requests are overdue—on average 101 days late—from FDA and HHS," the letter states. "The authority and integrity of Senate and committee process are being challenged and due concern should be shown to this nomination." Baucus, currently the ranking minority member on the Senate Finance Committee, is scheduled to take over as committee chairman.

Mark Cohen, food and drug safety director at the Government Accountability Project, a Washington watchdog group, said that while von Eschenbach didn't create the problems with Ketek, "he has adopted all of these problems and hasn't assisted those who were trying to seek a better outcome, and has aligned himself with the sources of the problem."

These problems date back to 2001, when the agency declined to approve the drug, citing safety concerns.

The company launched a new U.S. trial, but that study was marred by multiple protocol violations and outright fraud, which led to imprisonment of the top accruing physician. Nonetheless, the agency approved the drug in April 2004, labeling it for use in sinusitis, bronchitis, and pneumonia.

Congressional investigations began in late 2005, as whistleblowers came forward with reports of fraud in the registration trial, fatal liver toxicity, and FDA's approval of trials of the drug in children.

The agency's decision to stonewall Grassley appears to be strategic, Cohen said.

"I think they concluded two things about Congress prior to the November election: One, that Grassley didn't have enough backing in his own party and with sympathetic Democrats to enforce a subpoena that he might have issued as Senate Finance Committee Chairman, and that the House Democrats didn't matter

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at all," Cohen said. "So they completely blew them off. But, obviously, all of that has changed now."

Rep. Edward Markey (D-Mass.) and Rep. Henry Waxman (D-Calif.) are also investigating the Ketek affair.

Grassley has stopped von Eschenbach's plans before. Last year, when the Texas urologist and Bush family friend insisted that he would continue to run both NCI and the regulatory agency, Grassley objected repeatedly in letters to the administration.

"Atmosphere of Fear of Reprisal"

In a Sept. 20 letter to von Eschenbach, Grasley accused the FDA head of instilling an "atmosphere of fear of reprisal" at the agency.

"According to the FDA, there are regulations and procedures in place to help resolve organizational and individual disagreements," Grassley wrote. "However, my committee staff continues to hear from FDA employees who experience intimidation and reassignments when they raise concerns about the integrity of FDA's work."

Von Eschenbach apparently made himself an issue when he met with agency staff members involved in evaluating the Ketek application after The New York Times published a story based on internal FDA memoranda in which an agency official called for SanofiAventis to halt the Ketek trials in children.

"Your recent meeting with FDA staff involved in the review of Ketek is a disturbing example that FDA's internal dispute resolution processes are not working," Grassley wrote in the Sept. 20 letter. "Instead of reassuring FDA employees that they can raise concerns without being subjected to retaliation or intimidation, the meeting itself appears to be an act of intimidation. Scientists who speak up about problems and concerns, whether internally or externally, help ensure that our government operates efficiently, effectively, and in the best interest of the American people.

"FDA employees need to hear from the leader of the agency that they can freely voice their concerns without fear of reprisal."

The letter is posted at http://finance.senate.gov/press/Gpress/2005/prg092006.pdf. On Nov. 30, Grassley released the text of von Eschenbach's responses to his written questions.

One of Grassley's questions to von Eschenbach offers additional detail about the meeting:

"According to a number of FDA employees present, your speech used a lot of sports metaphors regarding being 'team players' and keeping opinions 'inside the locker room' and not voicing them outside the locker room. Apparently, among a number of troubling comments, you stated that a team member who spoke outside the 'locker room' might find themselves 'off the team' as a consequence."

In his response, von Eschenbach acknowledged having met with the agency's Ketek team, but said there was no intimidation (story on p. 4).

FDA said repeatedly that it was unable to respond fully to Grassley's subpoenas because it was conducting its own investigation.

"Another guy would have thrown the process under the bus to save his own hide, but he is not going to do that," said Robert Goldberg, vice president of the Center for Medicine in the Public Interest, a von Eschenbach supporter. "He does have the respect for the scientific process. He is committed to that. He is not going to let a politician usurp that function."

Ketek will be reviewed again by two FDA advisory committees at a meeting Dec. 14-15.

Flying At 40,000 Feet

Many of von Eschenbach's predecessors have been able to shield themselves from politics by claiming to allow the agency operate through science-based procedures. These commissioners could credibly claim that FDA scientists were making decisions that were not political.

After the Plan B imbroglio, this shield is no longer available to von Eschenbach.

His immediate predecessors who ran the agency under the Bush administration disregarded the recommendations of outside advisors and started an interminable process of "public comment."

The breakthrough came literally on the eve of von Eschenbach's confirmation hearing (The Cancer Letter, Aug. 4).

In his quest to be named FDA commissioner, von Eschenbach has emerged as someone who can single-handedly cut through the process. By the same token, he can plausibly be held personally responsible for the agency's actions, including actions of his subordinates.

This is an enormous political liability, especially for an executive who takes pride in managing from 40,000 feet and leaving ground operations to subordinates.

"Someone who isn't doing a very good job running the FDA doesn't recognize that other people in the FDA are also not doing a good job," said Sidney Wolfe, director of Public Citizen Health Research Group. "You could say that maybe he is acting this way because he

doesn't have the authority of a commissioner. But that's ridiculous. Particularly if you are looking forward to being commissioner, you should practice being FDA commissioner, and making decisions, and getting involved, and I don't see evidence of that with him."

The decision to approve the morning-after pill made von Eschenbach acceptable to the Democrats who were blocking his nomination, but infuriated social conservatives. The two Senators who immediately placed holds on his nomination have a 100% rating from Family Research Council, a conservative group.

"He took it upon himself personally to resolve the Plan B issue," Goldberg said. "And that's an example of no good deed goes unpunished. But this is Andy. Love him or hate him, Andy does things his own way. This is the Philadelphia street kid in him. He feels that he is the leader at FDA, and that means that he has to defend the right policy and the right approach of the agency."

Family Research Council was among the conservative groups that applauded Grassley's hold on the nomination on Nov. 16. Then, on Nov. 17, von Eschenbach further complicated his political situation by approving silicone breast implants.

This move has likely created another set of problems for von Eschenbach, as Feinstein responded with a public statement of concern about the move. "Serious questions remain about the long-term safety of these products," she said in a statement. "The FDA has a responsibility to carefully monitor the health and safety of women who use these implants."

Last month, Feinstein and Sen. Olympia Snowe (R-Maine) urged von Eschenbach to delay approval pending review of reports that Mentor Corp., the sponsor of the devices, hadn't made a full disclosure of data involving leakage from silicone gel implants.

Feinstein is the vice chair of C-Change, a cancer organization headed by former president George H.W. Bush, where von Eschenbach served as vice-chairman of the board.

Last spring Wolfe met with von Eschenbach and other FDA officials to discuss his concerns about the silicone implants.

"When we met with him over the breast implants, he said, 'I am sure that Dr. [Daniel] Schultz [Director Center for Devices and Radiological Health] has heard all of this,'" Wolfe said. "It was as though he wasn't really that interested.

"We were there for almost an hour," Wolfe said. "[Von Eschenbach] listened. He was very affable, very polite, but affability and politeness are no substitute for being competent, and that he is not."

Ironically, holds on von Eschenbach's nomination ensure his ability to stay in his job as acting commissioner.

Should the full Senate take a vote and reject him, the clock will begin to tick and, under the federal Vacancies Reform Act, von Eschenbach would be able to stay in his job for no more than another 210 days.

However, as long as the Senate fails to act on his candidacy, he can simply remain in his job.

FDA Head Says He Supports Free Speech In Agency At "A Proper Time, Place"

In a written response to questions from Sen. Charles Grassley (R-Iowa), FDA Acting Commissioner Andrew von Eschenbach said he hadn't attempted to intimidate whistleblowers after a story about pediatric trials of the drug Ketek appeared in The New York Times in June.

"My comments… did not address this subject, but rather the issue of my experience in organizations like FDA," von Eschenbach wrote in a response. At FDA, free expression of opinion "must lead to a conclusion and an action," which must be "organizationally supported and executed," he wrote.

The document was released Nov. 30.

The text of Grassley's question and von Eschenbach's answer follows:

Question: The insights of whistleblowers help keep agencies accountable.

When employees who voice concerns or who raise allegations of fraud, waste and/or abuse are retaliated against or are forced to assert their legal rights as a whistleblower, there is a chilling effect on other employees who see the consequences of speaking the truth.

By letter dated April 27, 2006, I wrote you regarding the committee's investigation of Ketek and requested that you advise FDA employees that: they have the right to speak directly and independently to Congress, or to a Committee of Congress, without interference from the FDA if they wish, in accordance with 5 U.S.C. § 7211.

Retaliation against these individuals, or any other FDA employees, who communicate with the committee in reference to Ketek will not be tolerated. Such conduct is further punishable by 18 U.S.C. § 1505 and false statements and perjury are likewise punishable pursuant to 18 U.S.C. § 1001.

Further, under 5 U.S.C. § 2302(b)(8), a federal

employee authorized to take, direct others to take, recommend or approve any personnel action may not take, fail to take, or threaten to take any personnel action against an employee because of protected whistleblowing.

Protected whistleblowing is defined as disclosing information which the discloser reasonably believes evidences: a violation of law, rule, or regulation; gross mismanagement; gross waste of funds; an abuse of authority; or a substantial and specific danger to public health or safety.

Please also note that P.L. 109-115 enunciates a government-wide prohibition on the use of appropriated funds to pay the salary of any federal official who prohibits or prevents or threatens to prevent or prohibit a federal officer or employee from contacting Congress, and "any punishment or threat of punishment because of any contact or communication by an officer or employee with a Member, committee or subcommittee."

Nonetheless, I understand that in June you held a meeting with FDA staff involved with Ketek.

According to a number of FDA employees present, your speech used a lot of sports metaphors regarding being "team players" and keeping opinions "inside the locker room" and not voicing them outside the locker room. Apparently, among a number of troubling comments, you stated that a team member who spoke outside the "locker room" might find themselves "off the team" as a consequence.

Your meeting with Ketek staff was held in the midst of an ongoing congressional investigation and followed a number of critical reports in the media about the FDA's handling of Ketek. It is apparent that some FDA employees were offended by your comments, found them highly questionable, inappropriate, and potentially threatening.

Personally, I am greatly troubled by your decision to hold this meeting at all, let alone making comments about kicking anyone off the team. For the record, state whether or not you believe your comments raised even the appearance of being inappropriate, chilling, and/or threatening?

What assurances can you provide that you take seriously that some FDA employees found your comments threatening and that all employees within the FDA will be protected and not subjected to retaliation?

Answer: Any FDA employee who has concerns about fraud, waste, and/or abuse has both the right and the responsibility to make those concerns known to organizational management, Agency leadership, and all appropriate authorities.

In public and in private, I have consistently affirmed my commitment to that principle and to providing protection to those who have the courage to exercise this important right and responsibility.

My comments at the meeting to which you refer did not address this subject, but rather the issue of my experience in organizations like FDA, in which leadership must promote a culture of diversity, including academic freedom in expressing differences of thought.

However, in an organization such as the Agency, that thought process has an important purpose and it must lead to a conclusion and an action. This is, in fact, the very process in which you engage in the Legislative Branch—rigorous debate and discussions occur at a proper time, in a proper place, in a proper fashion (the locker room, if you will).

However, this is a team effort, with universal respect for opinion and perspective, and once this open process leads to a decision being made (a law is passed, a drug is approved), that decision is organizationally supported and executed. FDA thrives on a scientific/academic decision-making process that welcomes, and in fact depends on, the vigorous exchange of diverse and differing opinions.

However, as a result of a healthy process such as this, many times a consensus, or majority, decision will be reached, with which an individual who was part of the decision-making process may not agree. For individuals who participate in this team activity, so to speak, there must be respect for the process and recognition that in some cases the opinion of the majority of their peers may take precedence over their own.

The entire document is posted at http://finance.senate.gov/sitepages/grassley.htm.

Drug Development:

Appeals Court To Reconsider Ruling On "Right" To Drugs

By Paul Goldberg

A federal appeals court last week vacated an earlier ruling that held that terminally ill patients have a constitutionally guaranteed right to obtain experimental drugs.

Now, the case will be heard again by the 10 judges who are members of the U.S. Court of Appeals for the District of Columbia Circuit.

In May, the decision in favor of the plaintiff, the Abigail Alliance for Better Access to Developmental

Drugs, was made by a three-judge panel.

FDA, a defendant in the case, appealed, and in a ruling Nov. 21, the court agreed to an en banc hearing. The parties are expected to file briefs early next year, and oral arguments are slated to take place in March 2007. The case was filed on behalf of the Abigail Alliance by the Washington Legal Foundation.

As the appeals court granted rehearing en banc, the three-judge panel that initially ruled in WLF's favor rejected FDA's challenge to the "standing" of the two plaintiffs, WLF and the Abigail Alliance for Better Access to Developmental Drugs, a patients-right group.

If the full appeals court concurs with the May ruling of the three-judge panel, terminally-ill patients would be allowed to gain access to experimental drugs that have completed phase I testing (The Cancer Letter, May 5).

The ruling held that the right to obtain phase I drugs was part of the Due Process Clause of the Fifth Amendment, which provides that "no person shall be… deprived of life, liberty, or property, without due process of law."

Judge Declines To Issue Injunction In Ortho v. Amgen

By Paul Goldberg

A federal judge declined to issue a preliminary injunction that would end the Amgen Inc. practice of "bundling" its growth factors Aranesp, Neopogen and Neulasta.

The plaintiff, Ortho Biotech, argued that bundling in this case constitutes an unfair trade practice that would result in irreparable harm to the company that makes Procrit, an erythropoietin that competes with Aranesp.

However, Judge Stanley Chesler of the U.S. District Court for the District of New Jersey ruled that Ortho, a unit of Johnson & Johnson, didn't demonstrate that it would face irreparable harm if Amgen continues to bundle its products.

The ruling means that the matter is set to be resolved at trial. "We intend to proceed with discovery and, ultimately, to a full trial on the merits of the case," J&J said in a statement. "We are committed to our position that Amgen's contracts with oncology clinics are anti-competitive and could have adverse consequences for physicians, the healthcare system and competition."

Amgen officials said the company's bundling practice isn't anticompetitive.

"We believe that Amgen does not engage in anti-competitive practices in the sale of Aranesp," David Scott, Amgen senior vice president and general counsel, said in a statement. "Oncologists look to the unique benefits Amgen's products offer and make the right decisions for patients. Amgen's contract terms support competition and lower prices. We now look forward to vigorously defending our position in court."

Under the Amgen bundling program, oncology practices can earn discounts if they meet target levels of sales of erythropoietin Aranesp, and white blood cell growth factors Neupogen and Neulasta. According to Ortho, the discounts constitute a strategy to force oncologists to switch from Ortho's Procrit if they want to receive discounts on Amgen monopoly products Neupogen and Neulasta.

The judge ruled that Ortho had failed to establish that it would be irreparably harmed if the bundling practice were allowed to continue. Irreparable harm in this case is defined as harm that cannot be adequately remedied by money damages.

"To be sure, Ortho might be less profitable during this period then it would be had the injunction been granted, but all of Ortho's alleged injuries flow from this alleged decrease in profits," the ruling states.

"In this case, it appears that any loss in profits, as well as any harm collaterally flowing from these loss of profits, can remedied by monetary damages at the end of a trial on the merits. This is especially true given that the antitrust statute provides for triple damages for any proven violations."

NCI Programs:

NCI, FNIH To Support Research On Childhood Cancer Targets

By Kirsten Boyd Goldberg

NCI and the Foundation for the National Institutes of Health have formed a program to support research to identify and validate therapeutic targets for childhood cancer.

The program, called the Childhood Cancer Therapeutically Applicable Research to Generate Effective Treatments (TARGET) Initiative, is needed because improvements in outcomes for childhood cancer have slowed, said Malcolm Smith, a medical officer in the NCI Cancer Therapy Evaluation Program. Smith described the new program to the NCI Board of Scientific Advisors, which formed a subcommittee to provide scientific oversight for the program.

TARGET will focus on three areas:

—High-throughput array-based technologies

to comprehensively characterize genomic and transcriptomic profiles for selected childhood cancers.

—Gene resequencing to identify genes that are consistently altered in specific childhood cancers.

—High-throughput RNA interference and small-molecule screening methods to identify and validate therapeutic targets.

TARGET will begin with a pilot project, a collaboration between the Children's Oncology Group, St. Jude Children's Research Hospital, the University of New Mexico, and NCI, Smith said. The project will try to identify therapeutic targets for high-risk acute lymphoblastic leukemia. The project is obtaining high-resolution genomic and transcriptomic profiles on about 240 leukemia cases. About 200 genes will be selected for resequencing.

The initiative will fund cooperative agreements or contracts in the following areas:

—Tumor/sample component with associated disease expertise.

—Genomic/transcriptomic characterization.

—DNA sequencing.

—RNAi and small molecule screens.

Smith said the estimated cost for the project would be $8.8 million over three years to focus on two cancer types. The role of FNIH will be to raise funds for the project from the private sector.

* * *

Analyzing Cancer Risk: NCI has posted a Web site designed to help people assess and understand their risk of developing cancer.

"Cancer Risk: Understanding the Puzzle" at http://understandingrisk.cancer.gov explains terms and provides information on lowering risk for six cancers. Also, the site includes a section on how to analyze new stories about cancer, to determine the accuracy and applicability of findings reported in the media.

NIH News:

NHGRI Funds Large-Scale Sequencing Centers

Three institutions have won cooperative agreements from the National Human Genome Research Institute for large-scale sequencing, the institute announced.

NHGRI and NCI said the three sequencing centers will devote a significant part of their efforts to The Cancer Genome Atlas Pilot Project, which is testing the feasibility of a large-scale, systematic approach to identify important genomic changes involved in cancer. The three centers, their principal investigators and FY 2007 funding levels are:

—Broad Institute Sequencing Platform, The Eli & Edythe L. Broad Institute of the Massachusetts Institute of Technology and Harvard University; Eric Lander; $48 million.

—Washington University Genome Sequencing Center, Washington University School of Medicine, Saint Louis; Richard Wilson; $41 million.

—Human Genome Sequencing Center, Baylor College of Medicine, Houston; Richard Gibbs; $27.6 million.

* * *

R01 Grant Applications Go Electronic Feb. 5

Beginning with the Feb. 5 standard receipt date, NIH will require applicants to submit all Research Project Grant R01 applications electronically. No paper applications will be accepted.

NIH is strongly encouraging all potential principal investigators to contact their central grants offices immediately to learn how their institutions are handling these application form and process changes.

NIH will host a training event on Dec. 5, available in-person and via Web cast and archived for later viewing: http://era.nih.gov/training/esub_120506/.

For more information on electronic grant submission, see http://era.nih.gov/ElectronicReceipt/.

Funding Opportunities:

Program Announcements

PA-07-054: Development of Assays for high Throughput Drug Screening. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-054.html. Inquiries: Min Song, 301-496-8783; songm@mail.nih.gov.

PA-07-074: Symptom Clusters in Cancer and Immune Disorders. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-074.html. Inquiries: Ann O'Mara, 301-496-8541; omaraa@mail.nih.gov.

PA-07-083: Basic and Translational Research in Emotion. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-083.html. Inquiries: Kevin Quinn, 301-443 1576; kquinn@mail.nih.gov.

PA-07-072: Biobehavioral Methods to Improve Outcomes Research. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-072.html. Inquiries: Paige McDonald, 301-435-5037; Mcdonalp@mail.nih.gov.

PA-07-098: Chronic Illness Self-Management in Children and Adolescents. R03. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-098.html. Inquiries: Ann O'Mara, 301-496-8541; Omaraa@mail.nih.gov.

PA-07-099: Chronic Illness Self-Management in Children and Adolescents. R21. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-099.html.

RFPs Available

VA-255-07-RQ-0063: Provide Tumor Registry Services for the VA Medical Center, Kansas City, Mo. Full text: http://www.fbodaily.com/archive/2006/11-November/24-Nov-2006/FBO-01185.

N02-RC-67018-56: Facility for Breeding, Housing and Handling Virus Infected Mice, Genetically Manipulated Mice and Chimeric Mice. Inquiries: Juana Diaz, 301-496-8613, Richard Hartmann, 301-496-8620.

In Brief:

City Of Hope Is Planning To Recruit 100 New Faculty

(Continued from page 1)

100 new faculty. **David Ann**, professor, Departments of Medicine, Molecular Pharmacology and Toxicology, at the USC Keck School of Medicine and School of Pharmacy, was named professor in the Department of Clinical and Molecular Pharmacology. **Nagarajan Vaidehi** was appointed professor in the Division of Immunology. She was director of the Biomacromolecular Simulations, Materials and Process Simulation Center at the California Institute of Technology. **Janice Huss** was named assistant professor in the Department of Gene Regulation and Drug Discovery. She was research assistant professor in the Center for Cardiovascular Research at Washington University School of Medicine in St. Louis. **Jeremy Stark** of Tulane University Health Sciences Center was appointed assistant professor in the Department of Radiation Biology. **Tiziano Barberi**, research associate scientist at the Laboratory of Stem Cell and Tumor Biology at Memorial Sloan-Kettering Cancer Center, was named assistant professor in the Department of Neurosciences. **Huiqing Wu** was named staff pathologist and assistant professor in the Division of Pathology. Wu completed his hematopathology, surgical pathology and research fellowship at Brigham and Women's Hospital and Harvard Medical School. **Piroska Szabo** was promoted to assistant professor within the Division of Molecular Biology. Szabo was recently awarded a five-year, $2.1 million grant from NIH to study epigenetic changes in fetal germ cells and fertility. . . . **MEMORIAL SLOAN-KETTERING** Cancer Center appointments: **James Fagin**, a thyroid cancer scientist, was named chief of the endocrinology service, Department of Medicine and a member of the human oncology and pathogenesis program. Fagin was director, Division of Endocrinology and Metabolism and Heady Professor of Medicine, University of Cincinnati College of Medicine. **Ronald DeMatteo**, hepatobiliary surgeon, was named vice chairman, Department of Surgery and head of the new Division of General Surgical Oncology. DeMatteo, who joined the hepatobiliary service in 1999, also is director of the fellowship training program in general surgical oncology. . . . **ASCO FOUNDATION** will award nearly $1 million to two scientists to pursue clinical and translational research in lung cancer. **Eric Haura** of H. Lee Moffitt Cancer Center and Research Institute and **Pierre Massion** of Vanderbilt University Medical Center will receive the 2007 Advanced Clinical Research Awards. Each will receive a three-year award totaling $450,000. The awards are supported by Genentech BioOncology. . . . **HOWARD FEDEROFF** was named executive vice president for health sciences and executive dean of the Georgetown University School of Medicine, effective April 1. He is senior associate dean for basic research and professor of neurology, medicine, microbiology, oncology and genetics, University of Rochester School of Medicine. . . . **CAROLYN HECKMAN** was named associate member, Division of Population Sciences at Fox Chase Cancer Center. Heckman was professor in the Departments of Psychiatry, Psychology and Internal Medicine at Massey Cancer Center at Virginia Commonwealth University in Richmond.

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THE CANCER LETTER

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Business & Regulatory Report

Product Approvals & Applications:

FDA Approves Herceptin For Adjuvant Treatment Of HER2, Node+ Breast Cancer

Genentech Inc. (NYSE:DNA) of South San Francisco said FDA approved Herceptin (Trastuzumab), as part of a treatment regimen containing doxorubicin, yclophosphamide, and paclitaxel, for adjuvant HER2-positive node-positive breast cancer.

The approval was based on interim joint analysis of 3,500 patients enrolled in two phase III trials. The addition of Herceptin to standard adjuvant therapy reduced the risk of breast cancer recurrence, the primary endpoint of the studies, by 52 percent (or a hazard ratio of 0.48) in HER2-positive breast cancer, compared to standard adjuvant therapy alone, the company said.

(Continued to page 2)

Clinical Trials:

CuraGen, TopoTarget Begin Phase II Trial Of PXD101 In Myelodysplastic Syndromes

CuraGen Corp. (NASDAQ:CRGN) of Branford, Conn., and **TopoTarget A/S** (Copenhagen Stock Exchange: TOPO) said they have begun dosing in a phase II open-label, multi-center trial evaluating the efficacy and safety of intravenous PXD101, a small molecule histone deacetylase inhibitor, for myelodysplastic syndromes.

The trial is sponsored by NCI under a Clinical Trials Agreement with CuraGen for PXD101, the company said.

Amanda Cashen, assistant professor, Washington School of Medicine in St. Louis, is leading the trial.

Up to 55 patients will be enrolled and receive five daily treatments of PXD101 administered by intravenous infusion every three weeks (one cycle), the company said. Those demonstrating complete or partial response will continue to receive treatment with the drug for up to eight cycles or until disease progression.

The primary endpoint is the proportion of confirmed responses as defined by the International Working Group, the company said. Secondary endpoints include the time to progression, overall survival, duration of response, and toxicity. The pharmacodynamic activity of the drug will also be evaluated by the assessment of histone acetylation, gene expression profiling and DNA methylation. Enrollment will be at multiple sites in the U.S., the company said.

"HDAC inhibitors modulate the expression of genes and have shown activity in eliciting a positive effect on MDS," Cashen said.

(Continued to page 4)

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FDA Approves Herceptin For Adjuvant Therapy

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"This is the largest improvement in outcome for any group of women with breast cancer in 25 years," said Edward Romond, professor of medicine, Division of Hematology/Oncology at the University of Kentucky.

After three-and-a-half years in the study, 87 percent who received treatment with Herceptin plus chemotherapy were disease free, compared to 71 percent treated with chemotherapy alone, the company said. A survival analysis conducted after a median of 24 months showed a 33 percent reduction in the risk of death (based on a hazard ratio of 0.67), which is equivalent to a 49 percent improvement in overall survival.

The two phase III trials were sponsored by NCI, and conducted by a network of researchers led by the National Surgical Adjuvant Breast and Bowel Project and the North Central Cancer Treatment Group, in collaboration with the Cancer and Leukemia Group B, the Eastern Cooperative Oncology Group and the Southwest Oncology Group, the company said.

The randomized, controlled trials consisted of four cycles of doxorubicin and cyclophosphamide followed by paclitaxel, either every three weeks or weekly for 12 weeks, compared with the same regimen plus 52 weeks of Herceptin beginning with the first dose of paclitaxel, the company said.

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BioCryst Pharmaceuticals Inc. (NASDAQ: BCRX) of Birmingham, Ala., said the European Committee for Orphan Medicinal Products, the European Medicines Agency, has granted Orphan Medicinal Product Designation to the anticancer drug Fodosine for T-Cell Acute Lymphoblastic Leukemia.

In 2005, FDA granted Orphan Drug designation for three indications: T-cell non- Hodgkin's lymphoma, including CTCL; CLL and related leukemias including T-cell prolymphocytic leukemia, adult T-cell leukemia, and hairy cell leukemia; and for B-ALL, the company said. Additionally FDA granted Fast-Track status to the development of Fodosine for relapsed or refractory T-cell leukemia.

In early 2006, BioCryst said it entered into a strategic collaboration with Mundipharma International Holdings Ltd. to develop and commercialize the drug in Europe, Asia, Australia.

Fodosine is a transition-state analog inhibitor of the target enzyme purine nucleoside phosphorylase, the company said.

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Bristol-Myers Squibb said the European Commission approved Sprycel (dasatinib, formerly known as BMS-354825) for adults with chronic, accelerated or blast phase chronic myeloid leukemia with resistance or intolerance to prior therapy, including imatinib mesylate.

The agent also is indicated for adults with Philadelphia chromosome positive acute lymphoblastic leukemia and lymphoid blast CML with resistance or intolerance to prior therapy, the company said.

Data from a European center study indicates that resistance to imatinib mesylate may occur in 2 percent of chronic phase CML patients, 41 percent of accelerated phase patients and 92 percent of blast crisis patients, the company said.

"Initial clinical trials demonstrate that Sprycel can affect leukemic cell growth enabling many adults with CML or Ph+ ALL to control their disease over a sustained period of time," said François Guilhot, professor of hematology, director of the Clinical Research Centre, University Hospital La Miletrie, Poitiers and president of the French Chronic Myelogenous Leukemia Group.

"In a phase II study, the drug demonstrated significant hematological and cytogenetic efficacy in imatinib mesylate-resistant and -intolerant CML patients in chronic phase; moreover, in the majority of patients with chronic phase CML who had become resistant to standard therapy, responses were durable. It is worth noting that as early as the phase I study, hematologic

and cytogenetic responses were observed in all phases of CML and in Ph+ ALL in the first 84 patients treated and followed for up to 19 months. Responses were durable across all phases of CML and Ph+ ALL," Guilhot said.

The EMA reviewed the efficacy and safety of Sprycel in five phase II multi-center studies for resistance or intolerance to imatinib mesylate in all phases of CML or Ph+ ALL, the company said. Sprycel was shown to have a predictable and manageable side-effect profile, the company said. In the 911 patients receiving the drug in clinical trials, the most common side effects were fluid retention, gastrointestinal, skin rash, headache, haemorrhage, fatigue, and dyspnoea.

The drug is available in Austria, Germany, France, Finland, Sweden and the U.K., the company said.

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Dendreon Corp. (NASDAQ:DNDN) of Seattle said the final portion of the Biologics License Application for Provenge (sipuleucel-T) has been electronically submitted to FDA, which completes its rolling submission that began in August.

Dendreon said it is seeking marketing approval for the agent for asymptomatic, metastatic, androgen-independent prostate cancer. As part of the submission, Dendreon said it has requested a Priority Review designation.

The BLA is based on a double-blind, placebo-controlled phase III study, known as D9901, which demonstrated that asymptomatic, metastatic, androgen-independent prostate cancer group treated with Provenge had a median survival time 4.5 months longer than the median survival seen in the group that received placebo, the company said.

Treatment with Provenge demonstrated a 41 percent overall reduction in the risk of death (p-value = 0.010; HR = 1.7). In addition, 34 percent receiving Provenge were alive 36 months after treatment compared to 11 percent randomized to receive placebo, the company said.

Provenge (sipuleucel-T), an investigational product, stimulates the immune system.

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Gendux AB of Stockholm, Sweden, and **Introgen Therapeutics Inc.** (NASDAQ:INGN) of Austin said they have reached agreement with the European Medicines Agency Committee to file for Advexin p53 therapy marketing approval under the EMEA Exceptional Circumstances provisions.

The application will be for Advexin p53 therapy for of Li-Fraumeni Syndrome, the companies said.

Gendux said also that Advexin has been confirmed by the European Commission as an Orphan Medicinal Product.

Introgen and Gendux have said that the drug therapy is available on a compassionate use basis to qualified LFS cancer patients.

Introgen and Gendux said they would complete the filing of Advexin applications for the European approval of LFS, the European approval for head and neck cancer, and the U.S. approval for head and neck cancer. The compatibility of EU and U.S. filing and submission requirements facilitate the achievement of the regulatory filing objectives, the companies said.

Advexin is a targeted molecular therapy with applicability in a range of tumor types and clinical settings because it targets abnormal p53 tumor suppressor function, associated with cancer initiation, progression and treatment resistance, the companies said.

The treatment has demonstrated increased survival and durable locoregional disease control in recurrent head and neck cancer, the companies said. Advexin also has demonstrated clinical activity in solid tumor types in multiple phase I, II and III trials. A request for accelerated approval review is pending at U.S. FDA. FDA has selected Advexin as a Fast-Track program for an unmet medical need and has designated the drug for orphan drug use for recurrent head and neck cancer.

* * *

Medicsight PLC (AMEX:MGT)of Chicago said it has received FDA 510(K) clearance for Medicsight ColonCAR 1.2.1, an image analysis software tool used with CT colonography for colorectal polyps.

The software tool uses a series of filters deployed against image data from CT colonography studies, the company said. The filters highlight spherical areas as small as 5mm.

Once suspected polyps are found, the software can determine the shape and features, precisely identifying the boundaries and showing the lesion in 3D with automatic diameter and volume measurements. This allows review and monitoring of the polyps over time, the company said.

The Medicsight ColonCAR software will be integrated within imaging 3D advanced visualization products from TeraRecon Inc., Viatronics Inc. and Vital Images Inc., the company said.

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Morphotek Inc. of Exton, Pa., said FDA has granted orphan drug status to MORAb-009, a monoclonal antibody, for pancreatic cancer.

MORAb-009 recognizes mesothelin, a cell surface

glycoprotein over-expressed in cancers, the company said.

NCI and Johns Hopkins University have independently validated the association of the protein in cancer and the therapeutic drugs that can target it, the company said. The data have shown a high correlation of mesothelin expression with pancreatic, mesothelioma, ovarian, non-small cell lung carcinomas as well as several epithelial-based cancers.

Clinical Trials:

Firms Also Testing PXD101 In Phase II For Ovarian Cancer

(Continued from page 1)

In a related development, CuraGen and TopoTarget A/S said they have begun a phase II trial, sponsored by NCI under a clinical trials agreement, evaluating the antitumor activity of intravenous PXD101 for ovarian cancer.

Amit Oza at Princess Margaret Hospital is leading the trial, the companies said.

Treatment will be for either advanced platinum resistant ovarian tumors or micropapillary/borderline low malignant potential ovarian carcinoma, the comany said. Patients may have received no more than three prior lines of therapy. Treatment will consist of intravenous PXD101 daily for five days in three week cycles until disease progression. The primary endpoint is the determination of objective disease response, as evaluated by the RECIST criteria. Secondary endpoints include evaluation of safety and tolerability of PXD101, stable disease rates, duration of response, progression-free survival, as well as median and overall survival. Up to 62 patients at sites across Canada and the U.S. will be enrolled, the company said.

"Hypoacetylation appears to play an important role in silencing the expression of genes, including tumor supressors that regulate cell survival, proliferation, and differentiation," said Oza. "The ability to reactivate tumor suppressor genes, together with the new published preclinical data, provides an excellent rationale to evaluate the role of the histone deacetylase inhibitor, PXD101 in treating two different populations of patients with ovarian cancer, those with advanced refractory tumors and those patients with micropapillary and borderline, or low malignant potential, tumors."

Correlative pharmacodynamic studies will also be conducted to evaluate the inhibition of HDACs in ovarian tumor cells from enrolled patients, the company said. Evaluation of the genes regulating proliferation and apoptosis, as well as acetylation of histone and non-histone proteins, will be performed.

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Berlex Oncology of Wayne, N.J., an affiliate of Schering AG, Germany (FSE: SCH; NYSE: SHR) said it has begun a phase II study for follicular B-cell lymphoma.

The randomized, open-label study is known as the Primary Evaluation Measuring Improved Efficacy of Rituximab with Sargramostim trial, or PREMIER trial. The trial is evaluating the efficacy and safety of combining therapy with the monoclonal antibody rituximab and the cytokine sargramostim compared to treatment with rituximab alone for relapsed follicular B-cell lymphoma, the company said.

"Previous studies have suggested that the combination of sargramostim with rituximab may substantially improve the treatment efficacy of rituximab in indolent lymphomas, without the use of chemotherapy and without increasing toxicity," said Peter McLaughlin, lead investigator and professor, Department of Lymphoma/Myeloma at M.D. Anderson Cancer Center. "The study seeks additional data to evaluate the efficacy and safety of this combination therapy."

In the Premier study, the primary objective is a comparison of the efficacy of rituximab plus sargramostim to rituximab monotherapy, as measured by confirmed and unconfirmed complete response (CR+CRu) rate at eight weeks, the company said. Treatment will consist of either four doses of rituximab 375 mg/m(2) administered intravenously once weekly for four weeks or the same rituximab regimen plus LEUKINE 250 mcg administered subcutaneously, three times weekly for eight weeks.

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Bionovo Inc. (BULLETIN BOARD: BNVI) of Emeryville, Calif., said FDA has accepted its protocol to begin a multi-center phase I/II trial of BZL101 for metastatic breast cancer.

The study would determine the maximum tolerated dose and evaluate the safety and efficacy of BZL101, the company said.

Recruitment and testing will take place at 10 clinical sites in the U.S., the company said. Debu Tripathy, director of the Komen/UT Southwestern Breast Cancer Research Program at the University of Texas Southwestern Medical Center will serve as the overall principal investigator, the company said. Tripathy was a lead investigator on Herceptin trials sponsored by Genentech.

Primary endpoint measured in the open-label, non-

randomized, dose-escalation trial will be response to therapy evaluated by the Response Evaluation Criteria in Solid Tumors, the company said. Secondary measures of efficacy will include duration of overall objective response, progression-free survival, overall survival, and patient-reported quality of life.

BZL101 is an oral drug that induces apoptosis through mitochondrial transmembrane potentiation

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Callisto Pharmaceuticals Inc. (AMEX:KAL) of New York said it has begun dosing in a multi-center, open-label phase II trial of Atiprimod for low to intermediate grade neuroendocrine carcinomas including advanced carcinoid cancers.

The first study site is the Hematology Oncology Services of Arkansas in Little Rock, under the direction of Brad Baltz, principal investigator.

The primary objective is to evaluate efficacy of the treatment for low to intermediate grade neuroendocrine carcinoma in those with metastatic or unresectable cancer and have either symptoms, despite standard therapy or progression of neuroendocrine tumors, the company said. After signing an informed consent, enrollees are required to complete two weeks of a symptoms diary to establish their symptoms baseline before dosing begins. Efficacy evaluations will include the measure of target lesions, and the quantization of symptom relief, the company said.

Atiprimod is an orally bio-available small molecule drug that displays multiple mechanisms of action, the company said. The drug has been shown to be antiangiogenic, inhibit secretion of VEGF and IL-6, elicit an apoptotic response, and inhibit phosphorylation of key kinases involved in tumor progression and survival including Akt and STAT3. The drug is in three clinical trials: a phase II trial in advanced carcinoid cancer, a phase I/IIa trial in relapsed or refractory multiple myeloma, and in a phase I/IIa trial in advanced cancer, the company said.

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Cellgate Inc. of Redwood City, Calif., said it has begun a phase II trial of CGC-11047, a polyamine analog that halts cell growth and induce apoptosis.

The 40-patient trial for metastatic hormone refractory prostate cancer has the primary endpoint of efficacy based on PSA response, the company said. Safety, tolerability and time to progression will also be evaluated. CGC-11047 will be administered intravenously as a single-agent by infusion once weekly for three weeks over a four-week cycle at a dose of 200mg.

"This patient population is a large one, consisting of men with limited alternatives for managing their disease," said George Wilding, director of the University of Wisconsin Comprehensive Cancer Center. "Providing an effective means of controlling the progression of their cancer without the toxicities associated with traditional chemotherapies would represent an important improvement in patient care."

Cellgate said its compounds displace polyamines from their natural binding sites and prevent cell replication. In two separate phase I trials, 20 patients with a variety of advanced solid tumors have been treated with CGC-11047 well tolerated with no dose-limiting toxicities reported.

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Cell Therapeutics Inc. (Nasdaq: CTIC; MTAX) of Seattle said enrollment on its PIONEER lung cancer trial, begun in December 2005, has been temporarily suspended to allow maturity of the data and assessment of differences in early cycle deaths observed between arms of the study.

While most of the deaths were attributed to disease progression, more complete data is required to analyze the difference, the company said. Patients who are on the trial will continue to be treated per the protocol.

Also, following recommendations from FDA, the company said it reviewed the demographic and estrogen data and will amend the study while enrollment is suspended. The study will be amended to focus on the primary efficacy endpoint of survival in women with normal estrogen levels; the subset of patients that demonstrated the greatest survival benefit in the STELLAR trials, the company said.

The PIONEER trial was designed to enroll 600 PS2 chemotherapy-naive women with advanced stage NSCLC, the company said. Each study arm would be randomized to receive either Xyotax (paclitaxel poliglumex), at a dose of 175mg/m2 paclitaxel equivalents, or paclitaxel, at a dose of 175mg/m2, once every three weeks. The primary endpoint is superior overall survival with several secondary endpoints including disease control, response rate in patients with measurable disease, time to disease progression, and disease-related symptoms.

Xyotax is a biologically-enhanced chemotherapeutic that links paclitaxel, the active ingredient in Taxol, to a biodegradable polyglutamate polymer, which results in a new chemical entity, the company said. When bound to the polymer, the chemotherapy is rendered inactive, sparing exposure of the normal tissue to high levels of unbound, active chemotherapy and its associated

toxicities.

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EntreMed Inc. (NASDAQ:ENMD) of Rockville, Md., said it has begun a multi-center, phase II trial with its clinical-stage drug candidate, Panzem NCD (2ME2 or 2-methoxyestradiol), for recurrent or resistant epithelial ovarian cancer.

The study will be conducted by the Hoosier Oncology Group, Indianapolis, with Daniela Matei, assistant professor, Department of Medicine, Division of Hematology/Oncology, Indiana University Cancer Center, as principal investigator.

Primary objectives will be safety, pharmacokinetics, tumor response rate, and progression-free survival, the company said.

Data from in vitro studies demonstrated that 2ME2 has activity against a variety of ovarian carcinoma cell lines including those resistant to other chemotherapeutic agents, the company said.

* * *

Exelixis Inc. (NASDAQ:EXEL) of South San Francisco said its licensee **Helsinn Healthcare SA** has discontinued enrollment in the becatecarin (XL119) phase III trial program in biliary tract tumors.

Exelixis in-licensed becatecarin from Bristol-Myers Squibb in 2001 and out-licensed it to Helsinn in June 2005, the company said. Despite some evidence of becatecarin activity, preliminary analysis of the trial data by an Independent Data Monitoring Committee indicated that the comparator agent 5-fluorouracil demonstrated a greater than expected survival benefit, making it statistically improbable that the final study results could achieve the planned objectives for the trial, Helsinn said.

Becatecarin is a small molecule, anticancer compound that has orphan drug designation in the U.S, and the E.U., the company said.

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Genta Inc. (NASDAQ:GNTA) of Berkeley Heights, N.J., said patient accrual has been completed in a randomized phase III trial of Genasense plus chemotherapy in untreated acute myeloid leukemia.

A minimum target of 500 patients was prospectively specified for accrual, a goal that has now been reached. The trial was conducted by the Cancer and Leukemia Group B and sponsored by NCI, the company said.

Treatment consisted of standard chemotherapy with daunorubicin and cytarabine, and receipt of Genasense or no additional therapy was randomized. Genasense was given during initial therapy and in two additional chemotherapy cycles after achieving complete remission to patients over the age of 59 with no prior chemotherapy treatment, the company said.

Primary endpoint is a comparison of overall survival; secondary endpoints include percent CR, remission duration, safety, and other assessments, the company said. The CALGB has also conducted a number of correlative laboratory tests, including measurements of Bcl-2, the biochemical target of Genasense.

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Genzyme Corp. (NASDAQ:GENZ) of Cambridge, Mass., said it has begun treatment in a phase II trial examining the safety and effectiveness of Clolar (clofarabine) in untreated, older adults with acute myelogenous leukemia who are unlikely to benefit from standard induction therapy.

This is the second clinical study of clofarabine in adults with AML this year, and would provide support for expanding the product label, the company said.

"While the outlook for children and young adults with AML has improved during the last three decades due to advances in chemotherapy and bone marrow transplant, the majority of AML patients are over the age of sixty years and not able to tolerate these curative approaches," said Harry Erba, of the University of Michigan Comprehensive Cancer Center.

The CLASSIC II trial will enroll 109 patients at 30 sites in the U.S, the company said. The primary endpoint is overall response measured as either complete response or complete response with incomplete platelet recovery. Secondary endpoints include duration of remission, disease free survival, overall survival, safety and thirty-day mortality rate, the company said.

Treatment will consist of an induction cycle of intravenous clofarabine administered as 30mg/m2 per day for five consecutive days, and based on response, may consist of up to five additional cycles of treatment at a dose of 20 mg/m2 per day for five consecutive days, the company said.

Clolar has Orphan Drug designation for adult and pediatric ALL. FDA also granted six months of extended market exclusivity to the drug under the Best Pharmaceuticals for Children Act.

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Posit Science of San Francisco said it has begun a phase I study in breast cancer to evaluate the effectiveness of its Brain Fitness Program for a condition known as "chemo-brain."

The program is a series of computer-based exercises designed to reverse losses in brain function, including memory loss, and to improve concentration, the company said.

Enrollees must either be post chemotherapy or taking chemotherapy, and report mental decline, the company said. Requirements include training on computers at home for one hour a day, five days a week for two months and participation in telephone interviews and questionnaires.

Data from a study at Baycrest Research Centre for Aging and the Brain confirmed that the condition of chemo-brain is caused by chemotherapy. Eighty-percent of cancer patients who undergo chemotherapy suffer from the condition which results in a deficit in cognitive function and affects quality of life by impairing ability to concentrate, make decisions and fulfill responsibilities, the company said.

* * *

PTC Therapeutics Inc. of South Plainfield, N.J., said it has begun a phase I multiple-dose study to evaluate escalating dose levels of PTC299 in healthy volunteers.

PTC299 is an orally bioavailable drug that modulates RNA-mediated protein expression to inhibit the production of vascular endothelial growth factor in tumors, the company said.

Preliminary results from a phase Ia escalating, single-dose safety and pharmacokinetic study confirmed the drug is orally bioavailable, well tolerated, and safely achieves the desired target plasma concentrations, the company said.

PTC299 was discovered through the PTC proprietary Gene Expression Modulation by Small-Molecules, or GEMS, technology by targeting the post-transcriptional processes that regulate VEGF formation, the company said.

GEMS is a proprietary screening technology that identifies small-molecules that modulate post-transcriptional control mechanisms, the company said. Compounds identified through the GEMS technology target processes that act through the untranslated regions of messenger RNA molecules.

Deals & Collaborations:

Introgen Obtains License To M.D. Anderson Patents

Introgen Therapeutics Inc. (NASDAQ:INGN) of Austin, TX, said it has obtained the exclusive, worldwide license to a portfolio of patents from **M. D. Anderson Cancer Center** for nanoparticles used to deliver biologically active proteins, polypeptides and peptides to cancer cells.

While peptides alone may be removed from circulation, requiring frequent administration and high doses, the nanoparticle-polypeptide formulations can increase therapeutic activity and protect against rapid degradation normally associated with peptide therapy, the company said. In addition, the peptide nanoparticles can include targeting molecules to enhance cellular uptake and to improve therapeutic efficacy.

Introgen said it has three therapeutic nanoparticle product candidates: INGN 401 (nanoparticle FUS-1), INGN 402 (nanoparticle p53) and INGN 403 (nanoparticle mda-7). INGN 401 is in phase I testing for metastatic lung cancer.

Introgen said it holds license agreements with M. D. Anderson Cancer Center to commercialize products based on licensed technologies, and has the option to license future technologies under sponsored research agreements.

The University of Texas Board of Regents owns stock in Introgen. The arrangements are managed in accordance with M. D. Anderson's conflict of interest policies, the company said.

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Biomira Inc. (NASDAQ:BIOM) (TSX: BRA) of Edmonton said it has acquired **ProlX Pharmaceuticals Corp.**, of Tucson and Houston to develop cancer therapeutics.

The acquisition will give Biomira a portfolio of oncology products, including Stimuvax and PX-12. Formerly known as BLP25 Liposome Vaccine, Stimuvax is a synthetic MUC1 peptide vaccine, which incorporates a 25-amino acid sequence of the MUC1 cancer mucin, encapsulated in a liposomal delivery system. PX-12 is an inhibitor of thioredoxin. Increased thioredoxin levels in cancer cells have been linked to proliferation of solid tumors, including colon, lung and gastric cancers.

Biomira said it will pay $3 million in cash and 17,878,000 shares of Biomira common stock in return for all of the outstanding stock of ProlX. A payment in Biomira common stock of $5 million is due upon the initiation of the first phase III trial of a ProlX product. Another payment in Biomira common stock of $10 million is due upon regulatory approval of a ProlX product in a major market, the company said.

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Calypso Medical of Philadelphia said it would collaborate with **IMPAC Medical Systems Inc.**, an Elekta company, on radiation therapy solutions for organ motion management.

The Calypso 4D Localization System provides an objective and continuous method to setup treatment and

monitor the patient during radiation delivery without adding ionizing radiation, the company said.

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EvoGenix Ltd of Sydney, Australia said it would collaborate with National Cancer Institute under a CRADA to develop antibody therapies against a new cancer target.

EvoGenix said it would provide tailored antibodies against PAMP and NCI would carry out testing and initial clinical evaluation of the anti-cancer therapeutics.

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Genomic Health Inc. (NASDAQ:GHDX) of Redwood City, Calif., said it has signed a national contract with **Aetna** for Oncotype DX, the Genomic test service that quantifies breast cancer recurrence and predicts chemotherapy benefit for early-stage breast cancer.

The agreement establishes payment rates across all of the Aetna plans for members with the disease, the company said.

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Medarex Inc. (NASDAQ:MEDX) of Princeton, N.J., said it expects to receive an undisclosed milestone payment from its licensing partner **Amgen Inc**. for the advancement of an antibody into clinical trials.

The antibody was developed using the Medarex UltiMAb technology and is the fourth UltiMAb-derived antibody in clinical development by Amgen, the company said.

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Radiation Therapy Services Inc. (NASDAQ: RTSX) of Fort Myers, Fla., said it has acquired MIRO Cancer Centers and Michigan Comprehensive Cancer Institute, a network of radiation therapy treatment centers in Southeastern Michigan.

The seven-facility network consists of two full service facilities, five satellite facilities and Certificates of Need to operate eight linear accelerators.

The network treats 100 patients per day and the facilities generate annual global revenues of $14.0 million, the company said.

Farideh Bagne will remain in a transitional executive management role to integrate the acquired facilities into the Radiation Therapy operating structure, the company said.

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Radiation Oncology Services of America said it would enter into a partnership with **Atlanta Oncology Associates** and a financial partnership with **MedCare Investment Fund III, Ltd**., to begin an outpatient services company.

The ROSA founding partners include physicians associated with two providers of radiation oncology services in Florida, Georgia and Tennessee, the company said. All the founding ROSA centers offer services including intensity modulated radiation therapy, image guided radiation therapy and high-dose rate brachytherapy.

Atlanta Oncology Associates own eight treatment centers in the Metropolitan Atlanta area, Georgia and the Florida panhandle. Four AOA facilities are affiliated with the Georgia Center for Total Cancer Care, the largest private oncology/hematology practice in the Southeast and a national leader in advanced cancer treatment and research.

"Partnership with ROSA offers us a unique opportunity to be part of the development of a clinical legacy," said Dale McCord, president and CEO of AOA. "By focusing on providing quality outcomes driven by evidenced-based care, ROSA will share the knowledge and best practices of leaders in the radiation oncology field across a national network of physician providers."

William Permenter, founder and medical director for Cancer Care Centers in the West Tennessee communities of Jackson, Dyersburg and Paris, is also a ROSA founding partner, the company said.

Collectively, the providers represent 11 radiation treatment facilities and 18 radiation oncologists, the company said.

Dennis Hallahan, is co-founder and senior medical advisor for ROSA. Hallahan is the Ingram Professor of Cancer Research and chairman of the radiation oncology department at Vanderbilt University. He on national boards including the National Institutes of Health Study Section for Radiation Biology and Therapeutics.

The ROSA board of directors is chaired by Harry Jacobson, co-founder of Renal Care Group and vice chancellor for health affairs at Vanderbilt University.

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Schering AG (FSE: SCH) of Berlin and **Stanford University** have started a joint research program to identify positron emission tomography tracers for tumor imaging.

Under the agreement, Schering said it would have the option to assume exclusive rights for the development and commercialization of such tracers.

Molecular imaging is a method of diagnosing early pathological changes in the body at the molecular level, before they can be diagnosed using other imaging procedures. This allows both early and precise detection and characterization of cancer and other diseases.