THE CANCER LETTER

Vol. 32 No. 30
Aug. 4, 2006

FDA's Plan B Proposal Fails To Impress Democrats, Angers Social Conservatives

By Paul Goldberg

The day before he faced a Senate committee considering his candidacy to head FDA, Andrew von Eschenbach announced a proposal for approval of the emergency contraceptive Plan B.

In a July 31 letter to Barr Laboratories, the sponsor of Plan B, von Eschenbach said that he had decided to stop the administrative rule-making process that blocked the application, and would be willing to consider approval for over-the-counter sale of the morning-after pill for women over 18.

Under the proposal, the company would have to agree to place Plan B into a risk-management program to make sure that the pill doesn't get in the

(Continued to page 2)

In Brief:

Carmona's Term As Surgeon General Expires; Stem Cell Initiative Funds 17 Research Grants

RICHARD CARMONA'S term as Surgeon General expired and Carmona left the post over the weekend of July 29-30, with no announcement from HHS, according to news reports. An internal memo by Assistant Health Secretary **John Agwunobi** said he regretted that Carmona's term expired. A letter Carmona wrote to Public Health Service officers circulated on Capitol Hill. In the letter, Carmona cited several accomplishments, including last month's report on second-hand smoke. . . . **TRI-INSTITUTIONAL Stem Cell Initiative**, which is comprised of Memorial Sloan-Kettering Cancer Center, The Rockefeller University, and Weill Medical College of Cornell University, announced stem cell research projects to be funded through a $50 million gift from The Starr Foundation. Seventeen projects have been approved for a total of $6.7 million over two years. The projects involve collaborations among research scientists from at least two of the three institutions and will explore the biology or therapeutic value of stem cells derived from humans or model organisms. The initiative supports stem cell research broadly, including studies of human embryonic stem cells--both those registered by the federal government and those that are not--as well as adult, fetal, and cancer stem cells, as well as stem cells from experimental animals. Earlier this year, the initiative awarded funds to each of the three institutions for development and expansion of core research facilities to derive, maintain, and characterize human embryonic stem cells, said **Kathleen Pickering**, executive director. . . . **JOHN HARTINGER**, NCI associate director for budget and financial management, retired July 31, after more than 40 years of federal service.

(Continued to page 7)

Plan B Dominates Hearing On Von Eschenbach For FDA

(Continued from page 1)

hands of young girls.

At the Aug. 1 hearing of the Committee on Health, Education, Labor and Pensions, Democrats dismissed this proposal as a politically motivated departure from evidence-based medicine and vowed to block any vote on von Eschenbach's candidacy until FDA takes action.

Social conservatives, by contrast, interpreted von Eschenbach's plan literally to mean that the morning-after pill would soon become available for over-the-counter sale. The rule-making process initiated by von Eschenbach's predecessor Lester Crawford could have dragged on for years. Now, suddenly, the process was stopped, and conservatives were furious.

"Dr. von Eschenbach has shown a history of ignoring any concern for women's health in exchange for political expediency," Tom McClusky, vice president of government affairs The Family Research Council, an influential conservative group, wrote in an Aug. 1 letter to Sen. Mike Enzi (R-Wyo.), chairman of the committee.

"Because of actions prior to, and as acting FDA Commissioner, FRC opposes his confirmation and reserves the right to score any vote in favor of his nomination negatively in our annual scorecard," McClusky wrote.

Since millions of conservative voters consult the group's Web site before heading to the polls, some Senators would now hesitate to support the administration's nominee.

Von Eschenbach's difficulties with conservatives began in 2002. In one of his first actions as NCI director, he approved a "fact sheet" that stated that no known link existed between abortion and breast cancer. After conservative members of Congress protested, von Eschenbach removed the fact sheet from the Web site and conducted a consensus conference that concluded that, indeed, no such link existed (The Cancer Letter, July 12, 2002; March 7, 2003).

In the letter to Enzi, FRC claims that "no honest hearing was given" to the anti-abortion groups, "and Dr. von Eschenbach ensured that no dissenting voices were heard in the final report" of the abortion and breast cancer conference. The letter is posted at www.frc.org/get.cfm?i=LH06H01&f=FR03G04

"It's very disappointing for us to see a Bush nominee to go through with something like this, especially when the president has just signed his first veto in favor of life, vetoing embryonic stem cell research, and now with a bill on his desk about minors being taken across state lines for abortions," said Bethanie Swendsen, a spokesman for FRC.

Another conservative group, Focus on the Family, stopped short of issuing statements on von Eschenbach, but a news dispatch posted on that group's website quoted the FRC letter.

"A man who has drawn the wrath of the pro-abortion movement and the pro-life movement is up for the post of FDA commissioner," Focus on the Family reported.

Washington insiders expect that von Eschenbach will receive a recess appointment that would allow him to bypass Senate approval and serve out the administration's term as FDA commissioner.

Clinton: "Your Qualifications Are Impeccable"

The confirmation hearing Aug. 1 gave the Senate committee the opportunity to examine the agency's failure to act on Plan B and raise questions about what critics describe as politicization of FDA. Yet, even Democrats who slammed von Eschenbach on Plan B praised his qualifications for heading the agency.

"I admired Dr. von Eschenbach's leadership [at NCI], especially on issues of genomics and nanotechnology," said Sen. Edward Kennedy (D-Mass.), the ranking member of the committee. "As a survivor of cancer himself, he has brought an important patient-centered perspective into the institute and [FDA]."

THE CANCER LETTER

® The Cancer Letter is a registered trademark.

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

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
Letters to the Editor may be sent to the above address.

Subscriptions/Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
General Information/FAQ: www.cancerletter.com

Subscription $355 per year worldwide. ISSN 0096-3917. Published 46 times a year by The Cancer Letter Inc. Founded Dec. 21, 1973, by Jerry D. Boyd.

Sen. Hillary Clinton (D-NY), who pledged to block von Eschenbach's nomination if it gets to the Senate floor, similarly praised his performance as NCI director.

"Your qualifications and your experience… are impeccable," Clinton said at the two-and-a-half-hour hearing. "You are caught, unfortunately, in a situation that gives great pause to many of us because of what it means for the direction of FDA."

By refraining from challenging von Eschenbach's four-year stewardship of NCI, Democrats forego the opportunity to question his reorganizing the institute for the pursuit of a blatantly unachievable and now apparently abandoned goal to "eliminate suffering and death due to cancer" by 2015. Similarly, von Eschenbach's controversial plan to expand reliance on biomarkers escaped questioning by the committee.

Clinton described her decision to block von Eschenbach's candidacy as a matter of principle.

"FDA is, and should be, the gold standard for drug safety and efficacy, and unfortunately, like so much of this government in the last five-and-a-half years, it has been turned into a political football, and you are on the field," Clinton said. "We are directing these questions to you, because, unfortunately, given the way things run around here, there are very few opportunities for us to take stands on principle and to point out to the public what is at stake, because—unfortunately—this is not just about Plan B…

"Once you start politicizing the FDA, there is no stopping," Clinton said. "And from my perspective it is essential that we draw the line, and we are drawing the line right here."

No vote on von Eschenbach's candidacy was taken at the hearing.

47,000 Comments (And a Year) Later

Testifying, von Eschenbach said it was purely a coincidence that the news of his decision to return to active consideration of Plan B appeared the day before his confirmation hearing.

"The reason this was done yesterday is that this has been a process that has been unfolding, and his been on the way, and by virtue of legal prescriptions and requirements, I did not disclose it to the public until I first notified the company of my decision, and that occurred yesterday morning," he said.

In a departure from standard practice, the agency's July 31 approvable letter to Barr Laboratories was made public on the agency's Web site. The document is posted at www.fda.gov/oc/planb/duramed073106.html.

The prospect of resolution of the Plan B controversy was similarly floated last year, when Lester Crawford's candidacy bogged down over the agency's failure to act on the application.

At that time, HHS Secretary Michael Leavitt promised in a letter that action on the application was imminent. This broke the logjam on the confirmation, but Crawford failed to deliver on the promise.

Before departing from the agency under circumstances that remain murky, Crawford launched an effort in rulemaking that took a year and generated an estimated 47,000 comments from the public. The majority of people and organizations who submitted comments said that no rulemaking was, in fact, needed, the agency said.

The most politically charged question in the Plan B controversy revolves around the agent's availability to young women.

FDA's advisors said in December 2003 that the morning-after pill should be made available for over-the-counter sale without an age restriction. However, the agency rejected the initial application by Barr Pharmaceuticals, the agent's sponsor, when it didn't mention the age limit.

When Barr returned with an alternative proposal to make the agent available for over-the-counter sale to women over 16, and by prescription to younger women, the agency responded that the age of eligibility should be pushed up to 17.

Shortly after making this proposal, FDA launched a lengthy, and critics say, transparently political rule-making process to deal with the regulatory questions purportedly raised by Plan B.

The current threshold, described by von Eschenbach, went up by another year, to 18. The letter to Barr doesn't offer any rationale for the new age limit. "[Because] of enforcement considerations, we believe that the appropriate age for OTC access is 18," states the document signed by von Eschenbach. "Should you desire to proceed with your [supplemental New Drug Application], you would need to amend it to seek approval for OTC status for women ages 18 and older."

A Barr spokesman said to The Cancer Letter that the company is scheduled to meet with the agency next Tuesday.

The Age of Plan B

Democrats had questions about von Eschenbach's Plan B proposal: What was the agency's rationale for raising the age of eligibility to 18? Was this based on

new data, expert opinion, or conservative politics? Why would the company and not the pharmacists be held responsible for ensuring that women buying the agent over the counter weren't, say, 17 and a half? Was the agency coming up with another tactic to delay the drug's availability and appease the administration's conservative supporters before the November election?

"Senator, I hope that you will accept the fact that I made this decision not on a political ideology, but on a medical ideology," von Eschenbach said in response to questions from Sen. Tom Harkin (D-Iowa). "The data is not there to suggest that 12-13 year-old girls can understand how to use this drug without medical supervision. Without that data being present, my ideology—and what I hope to always express as the Commissioner of the FDA—is to protect and promote their health and welfare. And the decision was made based on the fact that they should not have access to this drug without medical supervision. That's the ideology."

The idea to increase the risk management plan's age threshold from 17 to 18 was among the 47,000 comments the agency received on Plan B, von Eschenbach said. "The 18 year-old bifurcation was derived from the comments that came out of the process of rulemaking," he said.

Plan B wouldn't be the first FDA-regulated over-the-counter product to be made available to consumers over 18, von Eschenbach said. The nicotine replacement patches have the same age threshold.

Murray's challenge of von Eschenbach's actions on Plan B produced the most dramatic public grilling von Eschenbach has encountered since moving to Washington:

Murray: Is Plan B safe and effective for women who are 18 years old?"

Von Eschenbach: Plan B can be used safely and effectively.

Murray: Is it safe and effective for women who are 17.

Von Eschenbach: It can be used, but with medical supervision.

Murray: I have a letter from your predecessor from August 2005, that says that FDA found it safe over the counter for women ages 17 and older. Are you disputing that?

Von Eschenbach: Senator, what I am trying to communicate to you is I believe the drug can be used safely and effectively. I believe there needs to be a processes in place that reflect…

Murray: Last year, FDA found it safe and effective for women who are 17 and older. Yesterday, all of a sudden, you sent out a letter changing the age from 17 to 18. What new scientific or medical data about safety and effectiveness can you share to justify that change?

Von Eschenbach: That change was based primarily around our ability to manage this particular drug both by prescription and non-prescription.

Murray: So there is no medical and scientific data.

Von Eschenbach: There is no difference in the drug medically or scientifically. It's the ability to make sure that it's used safely and appropriately when it's [available] both by prescription and not by prescription.

Murray: But is it safe and effective for women who are 17 and under?

Von Eschenbach: It's safe and effective if it's used appropriately.

Murray: But you are holding this drug to a higher standard, and I would like to know where in the FDA charter is it that FDA should approve drugs based on behavior?

Von Eschenbach: I am sorry, Senator, I am not making this decision essentially holding it to a higher standard based on behavior… Once the drug is approved, as the opportunity currently exists, I must assure the safety and the protection of the women who will be using it.

Murray: Do you have data that it can't be used safely and effectively by women who are 17?

Von Eschenbach: The point of the data that was analyzed when the decision was made by the Center director, which I support, was that, in fact, the data was inadequate…

Murray: The letter that we have says that evidence does show—from a year ago, from your agency—that it's safe for 17.

Von Eschenbach: Senator, I've looked at the data. I reviewed…

Murray: So you've changed the FDA decision from a year ago.

Von Eschenbach: I've made this decision. I am of the opinion that, as it was judged by the center director, the data was insufficient to be able to ensure safe and effective use of this drug.

Murray: A year ago, it was safe for women who are 17, and now, all of a sudden, it's 18. I am pointing this out, because we need to show scientific data: this is why I did this. Let me ask you another question. I was really surprised yesterday to see that you wanted to place the

burden of enforcement on the manufacturer, and you said that if the manufacturer doesn't meet these standards, the FDA will deny the over-the-counter application for the agent. If pharmacists ignore the warning label or the manufacturer's instruction, who is to blame, pharmacist or the manufacturer?

Von Eschenbach: The application is to provide the drug across the continuum; prescription and non-prescription. In order to do that, it's my opinion that you must have proper risk management plan that the company did, in fact, submit with its application. As long as that risk management plan assures that you will protect…

Murray: I guess that's the question I am going for, and the concern that I have with your letter yesterday telling the manufacturer that if they can't prove that they can control the pharmacists, then all women will be denied the use of Plan B… So, basically, you are saying to women who are 25, and 35, and 45, that they will be denied the use of an effective drug. It's the question I raise, because it goes to the whole issue of the crisis of confidence we have in the FDA in making decisions based not on behavior, but on science, and that's my concern. And the second concern is, as you know, we've been down this road before. Right before a nominee is to be confirmed, we are told that a decision is imminent. You are talking about meeting with the manufacturer within the next seven days. But that's not a decision. That's looking for more information. That's exactly where we were one year ago today. And I want to know from you, what is the date certain that you will make a decision, yes or no?

Von Eschenbach: Senator, I hope you'll understand it, I view it as yesterday having made an important decision to not go forward with rulemaking…

Murray: To raise the age to 18… and then what?

Von Eschenbach: To invite the manufacturer to… address the elements of the risk management plan and we could then provide the risk management plan to assure a safe and appropriate use of this medication, high-dose hormone, so young girls who may not use it appropriately, because the data is inadequate, then we would go forward…

Murray: Is it not the case that if you meet with the manufacturer and decide to have a 90 day letter sent out…, you could do that, correct?

Von Eschenbach: It is my intent, Senator, to have the FDA meet with the manufacturer of this drug, to address the offer of this risk management plan, so we could move forward in a way that would provide this drug…

Murray: You can't give us the date certain?

Von Eschenbach: The exact date certain depends on the company and their discussions and negotiations. It's not something that I can guarantee… I hope that the facts that I outline in the letter creates in the company a very clear and very specific set of issues that they can immediately address, and if they do so, then this application will move forward.

A Slippery Slope

Susan Wood, former assistant FDA commissioner for women's health and director of the Office of Women's Health, who left the agency last year in protest over the handling of Plan B, said von Eschenbach's repeated references to the agent as a "high-dose hormone" were emblematic of the agency's strategy to focus on the drug's alleged toxicity.

In the past, FDA mandated risk-management programs exclusively for drugs that presented serious health risks. "There is no evidence of safety concerns about this product," Wood said to a group of reporters who gathered around her after the confirmation hearing. "To put the full force of the FDA safety concerns into this particular product is unnecessary, arbitrary and not appropriate for a product that is, in fact, very safe and very effective."

Wood is an advisor to the Reproductive Health Technology Project and a research professor at George Washington University School of Public Health and Health Services.

When top FDA officials first raised safety concerns about Plan B, they overruled a strong recommendation of outside advisors and consensus on all levels of the agency.

"The determination to cut out young teens at all was quite extraordinary, and was not based on safety concerns," Wood said. "There is no evidence of safety concerns of anyone on this product, and to raise that now as an assumption underlying keeping it out of the hands of younger teens—and this is now all the way up through age 17—is not based on the evidence. Is science and medical evidence driving this decision or not, and thus far I am not seeing that, unfortunately."

Wood said the agency's discussions with the sponsor could take a long time.

"All of these things take as long as it takes," she said. "If they come through with something in a week, I will be impressed, and I will not be surprised if it takes months."

At the hearing, Clinton said the agency's inaction

on Plan B appears to be motivated by desire to punish women who engage in risky sexual behavior. This sets a dangerous precedent, she said.

"Somebody could come in the future and say they disapprove of smoking," Clinton said. "So a new drug could treat lung cancer—directly related to smokers—shouldn't be approved, because those people should live with the consequences.

"Somebody could say, people need to start controlling eating habits, so drugs, interventions, and medical devices that deal with obesity, we shouldn't approve those. It's immoral that people get obese. This is a slippery, dangerous slope we are on, Doctor, and we are looking to you to get a decision made."

Kennedy, too, said he sees Plan B as a test case for the agency.

"We've seen FDA struggling with difficult scientific questions, inadequate resources, and unfair pressures to ignore science," he said. "FDA needs a strong commissioner to deal with these and other issues, to refocus the agency, enable it to make decisions based solely on science, developed under an open and unencumbered scientific disease, not on ideology or political expediency. So, Plan B is a test case of the FDA's integrity."

"Decisions Are Made With Judgment"

"Our workforce is my No. 1 priority," von Eschenbach said. "It's the most precious asset that FDA has."

Several Democrats cited last month's survey by the Union of Concerned Scientists, which suggests that the agency's morale problems stem from increasing politicization of its scientific review process.

Almost one in five of the scientists who responded to the survey indicated that they "have been asked, for non-scientific reasons, to inappropriately exclude or alter technical information or their conclusions in a FDA scientific document."

Other findings include:

—61 percent of the respondents said they knew of cases where HHS employees or FDA political appointees "inappropriately injected themselves into FDA determinations or actions."

—47 percent said that FDA "routinely provides complete and accurate information to the public."

—81 percent agreed that the "public would be better served if the independence and authority of FDA post-market safety systems were strengthened."

—70 percent disagree with the statement that FDA has sufficient resources to perform effectively its mission of "protecting public health…and helping to get accurate science-based information they need to use medicines and foods to improve their health."

The report is posted at www.ucsusa.org.

"This agency is really in trouble, and, some might say in crisis," Kennedy said at the Aug. 1 hearing. "At a time we are on the brink of the Life Science Century, with all the possibility that this has in terms of drugs. We need to have an agency that has the support of the administration, that has the support of Congress."

Sen. Barbara Mikulski (D-Md.), describing herself as "the Senator from FDA," said the agency is demoralized and losing key staff. "The scientists are hemorrhaging," she said. "They are leaving your agency."

Von Eschenbach acknowledged that the agency has problems with morale. "When there is a difference of opinion, we have in place guidances and processes for refutation, including the ombudsman process, so we can surface the difference of opinion and not have that become an issue where people fear that they will be penalized for voicing that opinion," he said.

Some of these concerns are overstated, von Eschenbach said.

"There is another issue, on the other side of it, and that is, when we talk about scientific deliberation or discussion, no one should ever alter the data or the scientific facts, but there are differences of opinion that arise with regard to interpretation of those facts, and that is an area where once consensus is arrived, if it doesn't happen to be one individual's point of view, it doesn't necessarily mean that that individual was right and the consensus was wrong," he said. "And because they protest or assume that somehow or other their point of view wasn't acceptable, it doesn't mean that the consensus was wrong… The data informs the decisions, but the decisions are made with judgment."

Von Eschenbach said his second priority at the agency will be to develop the Critical Path program that focuses on increasing reliance on biomarkers and development of adaptive designs for clinical trials.

"Through initiatives like Critical Path and Personalized Medicine, we are working to improve the tools we use, to more effectively evaluate new products and processes," von Eschenbach said in his testimony. "For example, through the use of biomarkers, we will be able to predict, earlier and more accurately, both the safety, as well as efficacy, of drugs, biologics and devices.

"This is the pathway that will take us into the era of personalized medicine, where health care is tailored to

each individual patient, and where the safety of medical products is enhanced by our improved understanding of how they interact with different patients, different drugs, and under different conditions."

Does science indeed stand on the threshold of personalized medicine? Is FDA the right agency to lead the way toward validation of biomarkers? How does the agency intend to proceed with this task?

A sustained and aggressive examination of these promises would have revealed a great deal about von Eschenbach's understanding of science, his controversial history at NCI—and his qualification to lead FDA.

In Brief:

NCI Budget Chief Hartinger Retires After 40 Years At NIH

(Continued from page 1)

Hartinger began his NCI career when the institute's annual budget was slightly more than $230 million, compared to the current $4.8 billion. As a branch chief in the budget office, Hartinger advised NCI directors Vincent DeVita, Samuel Broder, Richard Klausner, and Andrew von Eschenbach. Earlier this year, von Eschenbach established the John P. Hartinger Executive Leadership Development Award, an annual scholarship honoring an NCI employee who demonstrates leadership potential, a commitment to public service, and a desire to further his or her executive development. . . . **ALAN GLASSBERG** was named chief medical officer of Poniard pharmaceuticals. He was director of the company until last month. Previously, he had been associate director of clinical care and director of general oncology at the Comprehensive Cancer Center, University of California, San Francisco. Glassberg will work on moving picoplatin, the lead company product candidate, toward late-stage development and commercialization for small cell lung cancer and other solid tumors, said **Jerry McMahon**, chairman, president, and CEO of Poniard. Glassberg is on the board of directors of Biogen Idec and recently served on the board of directors of the National Comprehensive Cancer Network. . . . **DARELL BIGNER**, director of the Preston Robert Tisch Brain Tumor Center at Duke University, received the Honorary Degree of Doctor of Medicine at Lund University in Sweden. The degree is given to a prominent scientist who has collaborated with the University. Bigner, a leading authority on brain tumors, was recognized for his contributions to brain tumor research and for his long-standing collaboration with Swedish investigators. Bigner is also the Edwin L. Jones, Jr. and Lucille Finch Jones Cancer Research Professor and director of the Pediatric Brain Tumor Foundation Institute at Duke. He has received three consecutive MERIT awards from NCI for his research. . . . **MARVELLA FORD**, behavioral scientist and associate professor, Department of Biostatistics, Bioinformatics, and Epidemiology, Medical University of South Carolina, was named associate director for cancer disparities at the MUSC Hollings Cancer Center. MUSC HCC is planning to implement strategies to reach underserved and minority communities in the Charleston area with cancer early detection and treatment information. Ford, a researcher and behavioral scientist, has extensive experience in conducting cancer screening studies in diverse populations of older adults, said **Andrew Kraft**, HCC director. . . . **WILLIAM THORWARTH** will receive honorary membership in American Society for Therapeutic Radiology and Oncology during the annual meeting of the society in Philadelphia in November. He is being given the highest designation ASTRO can confer upon a leader in a discipline other than radiation oncology, said **Prabhakar Tripuraneni**, radiation oncologist at Scripps Clinic in La Jolla and chairman of ASTRO. Thosrwarth is being recognized for his support of radiation oncology in healthcare and political environments. Thorwarth joined Catawba Radiological Associated in Hickory, N.C., in 1984. . . . **DANIELLE SHAFER**, who specializes in leukemia and other hematologic cancers, has joined the Department of Medical Oncology at Fox Chase Cancer Center, as attending physician. Shafer completed a three-year fellowship in hematology and oncology at Fox Chase and was chief fellow from July 2005 to June 2006. She received the Amgen Hematology/Oncology Fellowship Grant in 2005. . . . **BEVERLY LORELL** and **M. KAY SCANLAN** will join the law offices of Washington-based King and Spalding's in their FDA healthcare practice. Lorell was vice president and chief medical and technology officer with Guidant Corporation. Scanlan was director of reimbursement strategy at Biogen and an adjunct professor of law at the University of Maryland where she taught Medicare and Medicaid law. The two senior advisors will work on pharmaceutical, medical device, biologics and food manufacturers on FDA and healthcare regulatory issues. . . . **ALLIANCE for Cancer Gene Therapy**, a charity that has funded $14 million in gene therapy research for all cancer types, will gather cancer scientists and clinicians for its fifth anniversary celebration dinner Sept. 18 in Greenwich. The keynote speaker will be **Judah Folkman**, director of the Vascular Biology

Program, Department of Surgery at Children's Hospital in Boston and founder of the field of angiogenesis research. NIH Clinical Center Director **John Gallin** will introduce Folkman. . . . **JIMMY FUND and Dana-Farber Cancer Institute** will be the beneficiaries of An Evening with Champions, a figure skating exhibition of Olympic and world skaters Oct 6, at Harvard University. The Jimmy Fund supports pediatric cancer research. For information, see www.aneveningwithchampions.org. . . . **CLARIFICATION**: Colorado became a smoke-free state on June 30, and thus the entire state qualifies to host meetings primarily sponsored by NCI under the institute's new smoke-free meetings policy (The Cancer Letter, July 21).

* * *

FIGHT ON, OLD FDA? FDA engineer **Gerald Harris** composed the "FDA Centennial Anthem" to commemorate the agency's 100th anniversary. The FDA Chorus, accompanied by the U.S. Public Health Service Wind Ensemble, performed the song June 30 at the agency's centennial celebration.

Here is the entire four-stanza song:

One century past, a people's hope fulfilled
By an act conceived for safe medicine and food
Protecting rights that our founding fathers willed
To life and liberty, to happiness pursued.

We honor those who carried on before
O'er these hundred years, public safety to secure
For food, vaccines, drugs, devices, blood and more
They strove to see these goods effective, safe, and pure.

In field and lab, in workplace far and near
From both civilian and commissioned corps
A call goes forth in this centennial year
That this rich heritage continue evermore.

Now in this proud hour, a vibrant vision thrives
True to our mission, whate'er the challenge be
With science our guide, we rededicate our lives
To help create a future healthy, safe, and free.

To read notes by Harris with discussion of each verse, see http://www.fda.gov/centennial/program/anthem.html.

* * *

ASCO's NEW HQ: American Society of Clinical Oncology held a ground-breaking ceremony Aug. 2 for construction on new ASCO headquarters, Carlyle Overlook, at 2318 Mill Road in Alexandria, Va.

ASCO occupies 74,000 square feet in three Alexandria office buildings. In the new space, ASCO will own and occupy 123,000 square feet on floors. The building is scheduled to be completed in March 2008.

"Today's ground-breaking is a historic milestone in ASCO's 42-year history," said Joseph Bailes, interim executive vice president and CEO. "While ASCO has leased office space in Alexandria for nearly a decade, the Carlyle Overlook is the first office space the society has ever purchased and will allow for all of our employees to be housed under one roof, supporting the current and future growth of the organization."

ASCO established its first headquarters in Alexandria in 1996. Since that time, membership has more than doubled and ASCO staff has increased from 18 employees to nearly 200 across 13 departments. Also, ASCO annual meeting attendance has increased from 12,000 to nearly 30,000.

Summer Publication Break

The Cancer Letter will not be published for the next three weeks while the staff takes its annual summer publication break. The next issue is scheduled for publication on Sept. 1.

Funding Opportunities:

RFAs, PAs Available

RFA-CA-07-027: Exfoliated Cells and Circulating DNA in Cancer Detection and Diagnosis. SBIR R43/R44. Letters of Intent Receipt Date: Aug. 26, Dec. 29, April 23. Application Receipt Date: Sept. 26, Jan 29, May 23. Full text: http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-027.html. Inquiries: Padma Maruvada, 301-496-3893; maruvadp@mail.nih.gov.

RFA-CA-07-028: Exfoliated Cells and Circulating DNA in Cancer Detection and Diagnosis. STTR R41/R42. Full text: http://grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-028.html.

PA-06-499: Exfoliated Cells and Circulating DNA in Cancer Detection and Diagnosis. R21. Application Receipt Date: http://grants1.nih.gov/grants/funding/submissionschedule.htm. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-499.html. Inquiries: Padma Maruvada, 301-496-3893; maruvadp@mail.nih.gov.

PA-06-500: Pathophysiology of Bisphosphonates-associated Osteonecrosis of the Jaw. R01. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-500.html. Inquiries: Roy Wu, 301-496-8866; wur@ctep.nci.nih.gov.

PA-06-501: Pathophysiology of Bisphosphonates-associated Osteonecrosis of the Jaw. R21. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-501.html.

PA-06-502: Pathophysiology of Bisphosphonates-associated Osteonecrosis of the Jaw. R03. Full text: http://grants.nih.gov/grants/guide/pa-files/PA-06-502.html.

Distribution Policy for The Cancer Letter

Thank you for your purchase of this issue of The Cancer Letter! Because issue and subscription sales are our major source of revenue, we wouldn't be able to provide you with the information contained in this newsletter without your support. If you have any questions or comments about the articles, please contact the editors (see page 2 of your issue for contact information).

We welcome your use of the newsletter and encourage you to send articles once in a while to colleagues. But please don't engage in routine distribution of The Cancer Letter to the same people week after week, unless your organization has purchased a site license or group subscription. If you aren't sure, ask the person who is paying for this subscription. If you are sending the newsletter to an unauthorized list, please stop; your actions are against Federal law. If you received this newsletter under an unauthorized arrangement, know that you are in receipt of stolen goods. Please do the right thing and purchase your own subscription.

If you would like to report illegal distribution within your company or institution, please collect specific evidence from emails or photocopies and contact us. Your identity will be protected. Our goal would be to seek a fair arrangement with your organization to prevent future illegal distribution.

Please review the following guidelines on distribution of the material in The Cancer Letter to remain in compliance with the U.S. Copyright Act:

What you can do:

- Route a print subscription of the newsletter (original only) or one printout of the PDF version around the office.
- Copy, on an occasional basis, a single article and send it to a colleague.
- Consider purchasing multiple subscriptions. We offer group rates on email subscriptions for two to 20 people.
- For institution-wide distribution or for groups larger than 20, consider purchasing a site license. Contact your librarian or information specialist who can work with us to establish a site license agreement.

What you can't do without prior permission from us:

- Routinely copy and distribute the entire newsletter or even a few pages.
- Republish or repackage the contents of the newsletter in any form.

If you have any questions regarding distribution, please contact us. We welcome the opportunity to speak with you regarding your information needs.

The Cancer Letter
PO Box 9905
Washington DC 20016
Tel: 202-362-1809
www.cancerletter.com

THE CANCER LETTER

Vol. 21 No. 7
July 2006

Business & Regulatory Report

Product Approvals & Applications:

FDA Approves Oncaspar In First-Line Treatment of Leukemia For Children

Enzon Pharmaceuticals Inc. (Nasdaq: ENZN) of Bridgewater, N.J., said FDA approved its supplemental Biologics License Application of Oncaspar (pegaspargase) as a component of a multi-agent chemotherapeutic regimen for the first-line treatment of acute lymphoblastic leukemia to include children as well as adults.

Oncaspar had been indicated for ALL when L-asparaginase is required in treatment, but where hypersensitivity has developed to the native forms, the company said.

(Continued to page 2)

Oncology Management:

M.D. Anderson Begins Patient Treatment At New Proton Beam Therapy Center

M. D. Anderson Cancer Center has begun treating patients at its Proton Therapy Center. M.D. Anderson said it is the first NCI-designated Comprehensive Cancer Center to offer the treatment. Altogether, four facilities in the US offer proton beam radiation.

The $125 million, 94,000-square-foot Proton Therapy Center is the most precise form of radiation treatment available for some tumors, said James Cox, head of the Division of Radiation Oncology at M. D. Anderson. Because of proton therapy precision, it minimizes harm to surrounding tissues and optimizes treatment of the tumor.

Protons differ from traditional x-ray treatment because they deposit the highest dose of energy when they come to a stop in the body, and have a very low dose of energy when they enter and have no dose as it exits the body, the center said. Proton therapy has proved most effective for cancers of the prostate, eye, lung, brain, head and neck and cancers in children.

Conventional radiation therapy, however, remains a proven and vital cancer treatment, and most often will still be the preferred radiation treatment, said Cox.

* * *

Cardinal Health Inc. (NYSE: CAH) of Dublin, Ohio, said it would acquire five PET radiopharmaceutical production facilities and manage a sixth site to manufacture and distribute PET radiopharmaceuticals.

The company said it would own facilities in Newark, N.J., Dallas, Texas, Memphis, Tenn., Birmingham, Ala., and Columbus, Ohio, formerly owned by Regional Nuclear Pharmaceuticals. A management agreement will be put

(Continued to page 3)

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

COG Study Found Oncaspar Could Be Used In ALL Regimen

(Continued from page 1)

Data in a randomized 118-patient multi-center trial conducted by the Children's Cancer Group, an NCI-funded cooperative oncology group and now incorporated under the Children's Oncology Group, demonstrated that the agent could be safely and effectively substituted for Elspar as part of a multi-drug cancer regimen, the company said.

Oncaspar is one of the first FDA-approved products that will come with prescription information in a new format designed to provide clear and concise information to health professionals, the company said.

"This treatment is a valuable alternative to current therapy," said Steven Galson, director of the FDA Center for Drug Evaluation and Research.

The use of Oncaspar in place of the currently used drug, L-asparaginase, reduces the number of drug injections required, from 21 injections of Elspar (L-asparaginase), which has been the standard of care, to three injections with Oncaspar over the 20-week course of treatment, the company said.

Serious side effects with the drug include anaphylaxis (allergic shock), other serious allergic reactions, blood clots, stroke, pancreatitis, glucose intolerance and bleeding problems, the company said.

* * *

Abbott of Abbott Park, Ill., said it received 510(k) clearance from the FDA for its automated, mid-volume hematology instrument, CELL-DYN Ruby.

With its advanced laser optics, the instrument enhances cellular analysis and efficiency for laboratories performing complete blood counts, the company said.

The CELL-DYN Ruby uses laser light to differentiate cellular components, the company said. Known as Multi-Angle Polarized Scatter Separation, this all-optical technology provides detailed results in easy-to-view diagrams, visually depicting changes in white blood cells, red blood cells and platelets.

The CELL-DYN family of hematology instruments range from larger analyzers that process a high number of patient samples to smaller instruments designed for medium and small-volume facilities. Besides supplying standard CBC results, some instruments have features to evaluate disease states or infections including cancer, HIV and anemias, the company said.

* * *

Bayer Pharmaceuticals Corp. (NYSE: BAY) of West Haven, Conn., and **Onyx Pharmaceuticals Inc.** (Nasdaq: ONXX) of Emeryville, Calif., said the European Commission has granted marketing authorization to Nexavar (sorafenib) tablets for advanced renal cell carcinoma where interferon-alpha or interleukin-2 based therapy has failed or the patient is unsuitable for such therapy.

Bayer said it would commercialize the drug in Europe.

The decision by the EC followed a positive opinion from the European Medicines Agency Committee on Medicinal Products for Human Use in April, the companies said. The agent was approved by the U.S. FDA in December 2005 and has since been approved in Switzerland, Mexico, Chile, Brazil, Korea, and Argentina. Regulatory filings have been completed in several countries, including Australia, Canada, Turkey, and Japan.

Nexavar EMEA approval was based on phase III data from the randomized, placebo-controlled trial for advanced renal cell carcinoma, the companies said. In the study, the treatment doubled progression- free survival in previously treated patients when compared to placebo. PFS was doubled to a median value of six months with the drug treatment as compared to three months with placebo (p-value < 0.000001). All subgroups examined, including those who had not received conventional treatment with biologics, such as interleukin-2 or interferon-alpha, appeared to benefit as well.

Nexavar is an oral multi-kinase inhibitor that

THE CANCER LETTER

Member, Newsletter and Electronic Publishers Association

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

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

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016

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

Business & Regulatory Report is a supplement to The Cancer Letter and available separately for $175 per year. ISSN 1053-9611.

targets both the tumor cell and tumor vasculature, the companies said. In preclinical models, the treatment targeted members of two classes of kinases, which included RAF kinase, VEGFR-1, VEGFR-2, VEGFR-3, PDGFR- B, KIT, and FLT-3.

* * *

GPC Biotech AG (Frankfurt Stock Exchange: GPC; TecDAX index; Nasdaq: GPCB) of Martinsried/ Munich said it has submitted the non-clinical section of the rolling submission of a New Drug Application to FDA for satraplatin in combination with prednisone as a second-line chemotherapy treatment for hormone-refractory prostate cancer.

"In the second half of 2006 we expect the final data on progression- free survival from our SPARC registrational trial and to complete the NDA filing by the end of 2006," said Bernd Seizinger, CEO of GPC Biotech.

Satraplatin, an investigational drug, is a member of the platinum family of compounds. Unlike other platinum drugs on the market, all of which require intravenous administration, satraplatin is an orally bioavailable compound and is given as capsules, the company said.

* * *

PharmaMar of Madrid said it has submitted a Marketing Authorization Application to the European Medicines Agency for Yondelis (trabectedin) for soft tissue sarcomas.

The application is based on the results of a randomised, phase II study of the drug, known as STS-201, the company said.

Yondelis was isolated from the marine tunicate Ecteinascidia turbinate, the company said. The treatment has a mechanism of action that binds into the minor groove of the DNA and interacts with DNA repair enzymes and transcription factors, interfering with different cell cycle processes.

In addition to STS, Yondelis is in a phase III trial for ovarian cancer and in a phase II for prostate and breastcancers, the company said. It was designated Orphan Drug status for STS and ovarian cancer by the European Commission and U.S. FDA.

The drug is being developed by PharmaMar together with Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

* * *

Pfizer Inc. of New York said Sutent (sunitinib malate) received European conditional marketing authorization for advanced and/or metastatic renal cell carcinoma, after failure of interferon alfa and interleukin-2 therapies.

The drug was given conditional approval for unresectable and/or metastatic malignant gastrointestinal stromal tumor after failure of the imatinib mesylate treatment due to resistance or intolerance, the company said. The efficacy is based on time to tumor progression and an increase in survival in GIST and an objective response rate for mRCC. The mRCC approval is conditional until the Committee for Human Medical Products reviews phase III study data, which Pfizer said it would submit in August.

Sutent is an oral therapy that inhibits inhibits both tumor growth and blood supply, the company said.

"To have 35 percent of patients in the study respond to the treatment is truly remarkable," said Sylvie Negrier, professor of medical oncology at Centre Leon Berard, Lyon, France. " Also, a large majority of patients were able to control their disease over time, signs of Sutent's significant effects in patients fighting kidney cancer."

Sutent has been granted Orphan Drug designation in the European Union for both advanced kidney cancer and GIST, the company said.

Oncology Management:

OTN Begins Web-Based Inventory, Reporting Tool

(Continued from page 1)

in place at a sixth site in Jackson, Miss., which was formerly managed by RNP. Through the agreement, Cardinal Health said it would gain ownership of five cyclotrons and related lab equipment to produce fluorodeoxyglucose- the primary radiopharmaceutical used in PET diagnostic imaging.

* * *

OTN of South San Francisco said it had launched of Lynx Mobile, an automated charge capture, inventory management and reporting tool.

The Web-based device was developed for community-based infusion therapy clinic staff to manage drug inventory and supplies and improve practice revenue management, the company said.

"Lynx Mobile has had a significant financial impact on our practice," said Sara Green, nurse manager/ practice administrator at Olympic Hematology & Oncology Associates, a full-service oncology practice in Bremerton, Wash. "It has allowed us to find, on average, three lost charges per day. We also have been able to efficiently manage our inventory levels to reduce our costs and greatly simplify our ordering process. "I and

our oncology nurses use Lynx Mobile daily because it is easy to use, convenient and available anywhere we need access, including at a wireless station in the middle of our patient treatment area."

* * *

RITA Medical Systems Inc. (Nasdaq: RITA) of Fremont, Calif., said it has begun U.S. sales for the LC Bead, a minimally invasive embolization technology for cancerous liver tumors.

Medicare and Medicaid will reimburse use of the LC Bead for the embolization of hepatocellular carcinoma, the company said. Reimbursement includes $1500 per procedure for physicians and a Medicare national average of $6400 in facility fees for each in-patient embolization procedure. FDA cleared the LC Bead for the embolization of hypervascular tumors and arteriovenous malformations in the U.S.

RITA said it has an exclusive three-year supply and distribution agreement with the manufacturer, Biocompatibles International plc of the U.K., to market the product in the U.S. and Canada.

Clinical Trials:

AnorMED's Phase III Trial Completes Enrollment

AnorMED Inc. (AMEX: AOM; TSX: AOM) of Vancouver said it has completed enrollment for one of two phase III trials of Mozobil for stem cell transplant in multiple myeloma.

The first trial reached its target enrollment of 300 and recruitment continues for the second phase III trial in non-Hodgkin's lymphoma, having enrolled 241 of the targeted 300 patients, the company said.

The two phase III trials are evaluating Mozobil in a standard stem cell mobilization regimen, the company said.

In accordance with the trial design, transplants will begin over the next 4-6 weeks with a subsequent 100 day follow-up period required, the company said. The MM trial design also allows physicians to request, upon enrollment, that a patient has the option to have a second or tandem transplant should they not go into complete remission. Physicians have up to 6 months from the first transplant to perform a second transplant if required. The 100 day follow-up period would then commence from the date of the second transplant. The results of the study will be unblinded once enrollment has occurred and 100 day follow-up has been completed. The tandem option is not available in the NHL trial, the company said.

Mozobil, a stem cell mobilizer used in stem cell transplants, triggers the rapid movement of stem cells out of the bone marrow and into circulating blood, the company said. Once in the blood, the stem cells can be collected for use in a stem cell transplant.

* * *

Cell Genesys Inc. (Nasdaq: CEGE) of South San Francisco said it has expanded a multi-center phase I trial of CG0070 to evaluate escalating multiple-dose regimens of CG0070 for recurrent bladder cancer.

The expanded trial will include up to 45 additional patients who have failed previous therapy with Bacillus Calmette-Guerin, the company said.

The open-label, dose-escalation trial is evaluating intravesical administration of the treatment and was designed to first evaluate escalating single-dose levels of CG0070 and has now been expanded to evaluate escalating multiple-dose regimens, the company said. The primary endpoints are safety and the determination of a maximum tolerated dose. Other endpoints include clinical response based on follow-up cystoscopy and recurrence-free survival.

The expansion of the trial from single-dose to multiple-dose regimens was prompted by anti-tumor activity documented by a complete response at follow-up cystoscopy at approximately three months in three of the nine patients evaluable to date. The duration of the complete responses after just a single administration of CG0070 were 6, 9, and 3+ months respectively. Treatment was generally tolerable and the majority of treatment-related side effects were local bladder toxicities. No serious adverse events or dose-limiting toxicities have been reported, the company said.

* * *

CuraGen Corp. (Nasdaq: CRGN) of Branford, Conn., and **TopoTarget** A/S (Copenhagen Stock Exchange: TOPO) of Denmark said they have begun dosing in a phase I/II trial evaluating the safety and efficacy of PXD101, a small molecule histone deacetylase inhibitor for inoperable hepatocellular cancer.

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

The open-label study is led by Winnie Yeo, Department of Clinical Oncology, Chinese University of Hong Kong, Prince of Wales Hospital in Shatin, Hong Kong, the company said. The phase I portion would establish the maximum tolerated dose, pharmacokinetics, and safety profile of PXD101, the company said. Fifteen patients will be enrolled in the dose escalation portion

and receive PXD101 in continuous three week cycles until disease progression. Following determination of the MTD, the phase II portion will be initiated and enroll up to 29 additional patients to assess the safety and potential efficacy of PXD101, the company said. Assessment of tumor response will be evaluated using the RECIST criteria. Secondary pharmacological studies evaluating histone acetylation, induction of cell-cycle arrest or apoptosis, and changes in gene expression will be conducted in a subset of enrolled patients, the company said.

The drug is in multiple clinical trials as a treatment for multiple myeloma, T-cell lymphoma, and colorectal and ovarian cancers, either alone or in combination with anti-cancer therapies, the company said.

In 2004, CuraGen said it signed a Clinical Trials Agreement with the NCI under which NCI will sponsor clinical trials to investigate PXD101 for various cancers, both as a single-agent and in combination chemotherapy regimens. In 2005, TopoTarget said it signed a CRADA with NCI to conduct pre-clinical and non-clinical studies on PXD101 to better understand its anti-tumor activity and to provide supporting information for clinical trials.

* * *

Cytogen Corp. (NASDAQ:CYTO) of Princeton said the NCI Radiation Treatment Oncology Group has initiated a randomized phase III trial to evaluate either Quadramet (samarium Sm-153 lexidronam injection) or strontium-89 chloride in conjunction with zoledronic acid (Zometa) for osteoblastic metastases from lung, breast, and prostate cancer.

The 350-patient study would determine if the addition of a radiopharmaceutical to bisphosphonates for asymptomatic or stable symptomatic bone metastasis will delay the time to development of malignant skeletal related events, defined as a pathological bone fracture, spinal cord compression, surgery to bone, or radiation to bone, the company said.

* * *

Genmab A/S of Copenhagen said it has begun a study of Ofatumumab (Humax-Cd20) for follicular non-Hodgkin's lymphoma refractory to rituximab.

The 162 NHL patient-study refractory to rituximab in combination with chemotherapy or to rituximab given as maintenance treatment, will be randomized into two dose groups, the company said. Each dose group will receive one infusion of 300 mg of HuMax-CD20 followed by 7 weekly infusions of either 500 or 1000 mg of HuMax-CD20. Disease status will be assessed every 3 months until month 24.

The study would determine the efficacy and safety of two dose regimens of the product. The primary endpoint is objective response as measured over a 6 month period from start of treatment assessed by an Independent endpoints Review Committee according to the standardized response criteria for non-Hodgkin's lymphomas.

* * *

Human Genome Sciences Inc. (Nasdaq: HGSI) of Rockville, Md., said it has initiated dosing in a randomized phase II trial of HGS-ETR1 (mapatumumab) in combination with bortezomib (Velcade) for advanced multiple myeloma.

"Bortezomib, a proteosome inhibitor, is indicated for multiple myeloma patients who have received at least one prior therapy," said Stefano Tarantolo, study investigator and medical oncologist, Nebraska Methodist Cancer Center, Omaha. It has produced partial or complete responses in approximately 50 percent phase II and III trials.

The primary objective is to evaluate disease response to HGS- ETR1 in combination with bortezomib, versus bortezomib alone, the company said. 100 patients will be enrolled in the U.S. and Canada and randomized into two treatment groups, with one treatment group receiving the combination of HGS-ETR1 and bortezomib, and the other treatment group receiving bortezomib alone. Secondary objectives are safety and tolerability, and to determine plasma concentrations of HGS-ETR1 for use in a population pharmacokinetic analysis.

HGS-ETR1 is an agonistic human monoclonal antibody that binds to the TRAIL receptor-1 protein and triggers apoptosis, in cancer cells, the company said.

HGS-ETR1 was generated through a collaboration between HGS and Cambridge Antibody Technology. GlaxoSmithKline has exercised its option under a June 1996 agreement to develop and commercialize HGS-ETR1 jointly with HGS. Under the agreement, GSK and HGS will share equally in phase III/IV development costs, and will share equally in sales and marketing expenses and profits of any commercialized product, under a co-development and co-promotion agreement, the remaining terms of which are being negotiated.

* * *

INB:Biotechnologies Inc., a wholly owned subsidiary of Integrated BioPharma Inc. (AMEX: INB) of Hillside, N.J., said it has begun dosing in a phase I trial of PhytoSel, a proprietary plant-derived oral formulation of selenium, to reduce side effects of two chemotherapeutic drugs.

The study will be conducted at City of Hope,

and lead by Stephen Shibata, Department of Medical Oncology & Therapeutics Research at City of Hope, the company said.

* * *

Oncolytics Biotech Inc. (TSX: ONC, Nasdaq: ONCY) of Calgary said it has completed enrollment in its phase Ib U.K. trial of Reolysin in combination with radiation therapy for advanced cancers.

The trial will treat with a range of two to six intratumoral doses of Reolysin at 1x10(10) TCID(50) with a constant radiation dose of 36 Gy in 12 fractions, the company said.

Enrolment in the phase Ia combination Reolysin/ radiation trial was completed in June, the company said. That trial tested two intratumoral treatments of Reolysin at dosages of 1x10(8), 1x10(9), or 1x10(10) TCID(50) with a constant localized radiation dose of 20 Gy given in five fractions. A maximum tolerated dose was not reached and the combination treatment appears to have been well tolerated. Preliminary analysis has demonstrated evidence of both local and systemic response, the company sad.

The phase Ib trial would determine the MTD, dose limiting toxicity, and safety profile of the drug when administered intratumorally to patients receiving radiation treatment. A secondary objective is to examine any evidence of anti-tumor activity. Eligible patients include those who have been diagnosed with advanced or metastatic solid tumors that are refractory to standard therapy or for which no curative standard therapy exists. An additional group would be treated at the maximum dose regimen reached in the Ib trial, the company said.

The principal investigators for the trial are Kevin Harrington of the Targeted Therapy Laboratory, The Institute of Cancer Research, Cancer Research U.K. Centre for Cell and Molecular Biology and Honorary Consultant in Clinical Oncology at The Royal Marsden NHS Foundation Trust, London, U.K., and Alan Melcher of the Cancer Research U.K. Clinical Centre at St. James's University Hospital in Leeds.

In another development, **Oncolytics Biotech Inc**. said it has begun enrolment in a phase I/II trial of Reolysin for recurrent malignant gliomas.

The principal investigator James Markert, Division Director of Neurosurgery, and professor, neurosurgery and physiology, University of Alabama at Birmingham, the company said.

The open-label dose escalation trial will treat with a single dose of Reolysin administered by infusion, the company said. Administration involves the stereotactically-guided placement of a needle into the tumor, through which the agent will be infused into the mass and surrounding tissue using a pump. The objective of the study is to determine the maximum tolerated dose, dose limiting toxicity and safety profile of the drug. Secondary objectives include the evaluation of viral replication, immune response to the virus and any evidence of anti-tumor activity.

* * *

Roche of Basel, Switzerland, said its international phase III randomized study NO16966 of 2, 035 untreated metastatic colorectal patients, met both primary endpoints.

The primary objectives were to answer two questions: whether the Xelox regimen is non-inferior to Folfox and secondly whether the addition of Avastin to chemotherapy is superior to chemotherapy alone. The secondary endpoints included overall survival, overall response rates, and safety profile, the company said.

Results showed that the chemotherapy combination Xeloda plus oxaliplatin, called Xelox is as effective for progression-free survival as infused 5-FU/leucovorin plus oxaliplatin, called Folfox, the company said.

The addition of Avastin to chemotherapy, Folfox and Xelox, improved progression-free survival compared to chemotherapy alone. Some variability in treatment benefit was observed in subgroups. No new safety signals related to Avastin were observed in the trial, the company said.

Results from the study will be submitted to a future international cancer congress, the company said.

* * *

Serenex Inc. of Durham, N.C., said it has begun a phase II trial of SNX-1012 for of chemotherapy-induced oral mucositis.

The study will compare multiple doses of the agent against a placebo control, the company said.

SNX-1012 targets multiple inflammatory and other pathways in the pathophysiology of oral mucositis, the company said. The product is administered as a topical, transmucosal agent as an oral rinse that interferes with many of the biological targets necessary for mucositis development. Four phase I trials have been, including a phase Ib study at the Fred Hutchinson Cancer Center, which showed strong indications of pharmacological activity and an excellent safety profile, the company said.

* * *

ZymoGenetics Inc. (Nasdaq: ZGEN) of Seattle said it has begun a phase I trial using Interleukin 21 in combination with the monoclonal antibody Rituxan for

non-hodgkin's lymphoma.

The U.S. multi-site open label dose-escalation trial will treat with Rituxan and IL-21 once weekly for four weeks, the company said. Responding patients will be offered the combination regimen for four additional weeks.

The objective is to evaluate the safety and tolerability of IL-21 when administered with Rituxan. Secondary objectives are to characterize the pharmacokinetics, immunogenicity and preliminary evidence of tumor activity of this combination, the company said.

Preclinical research with the combination demonstrates that IL-21 enhances a principal mechanism by which Rituxan is thought to work: IL-21 enhances the Rituxan-mediated killing of B-lymphoma cell lines, the company said. In the studies, after 90 days of follow-up, a combination of IL-21 plus low-dose Rituxan enabled survival of 70 percent of mice injected with an aggressive non-Hodgkin's lymphoma cell line, compared with only 10 percent that were treated with the same dose of Rituxan alone, and none that were treated with IL-21 alone.

Deals & Collaborations:

NCI Picks BioFortis Software For Intramural Research

BioFortis of Baltimore said **NCI** has selected its software, Labmatrix, for the NCI Center for Cancer Research, its intramural translational research program.

Labmatrix, a web-based, enterprise translational research information management software product, would integrate clinical data with genomic, proteomic and laboratory experimental data, as well as maintain annotated tissue banks, the company said.

The CCR decision to adopt the Labmatrix technology came after user evaluation within the Neuro Oncology Branch, the company said An analysis also was conducted of requirements needed to interface with existing CCR infrastructure utilizing caBIG interoperability standards. Existing infrastructure included clinical trials data management, patient registry and reporting systems, the company said.

* * *

Evotec AG (Frankfurt Stock Exchange: EVT, TecDAX30) of Hamburg said **DAC**, a wholly owned subsidiary of Genextra SPA, has chosen Evotec as a partner in a pharmaceutical discovery project on the HSP90 target, a protein implicated in oncogenic pathways in cancer.

Under the agreement, DAC would access compound intellectual property that Evotec has generated through its internal R&D activities, the company said. The collaboration would identify compounds and optimise them to clinical development.

Using its proprietary fragment screening platform, High Throughput Fragment Screening, Evotec said it had identified fragments that interact with the HSP90 target from its five thousand member fragment library. Active fragments were further characterised by co-crystallisation with the target protein. The X-ray crystal structures of the protein-ligand complexes identified a variety of binding modes some of which will give rise to novel approaches for inhibiting HSP90.

In the collaboration, which may run for over 2 years, Evotec said it would use its medicinal chemistry, profiling and Absorption, Distribution, Metabolism, Excretion and Toxicity expertise to generate lead molecules for further progression into clinical trials.

* * *

Extensity of Atlanta said it has a contract with **Dana-Farber Cancer Institute** for MPC financial performance management software to automate its operational, capital, and research budgeting processes.

* * *

Genentech Inc. (NYSE:DNA) and **Inotek Pharmaceuticals Corp**. said they have entered into an exclusive global collaboration to discover, develop, manufacture and commercialize inhibitors of poly (ADP-ribose) polymerase (PARP) for the potential treatment of cancer.

PARP is a nuclear enzyme within cells that directs the repair of damaged DNA via the activation and recruitment of DNA repair enzymes and has applications for the treatment of oncology and cardiovascular conditions.

Under the agreement, Genentech will make an upfront payment of $20 million to Inotek, with the potential for up to $405 million in additional milestone payments based upon the successful completion of various clinical development and regulatory events across multiple cancer indications in multiple areas of the world. Genentech will pay Inotek royalties based on the net amount of any sales of Inotek's lead PARP Inhibitor, INO-1001, or other next-generation PARP inhibitors in the field of cancer. Genentech will also provide funding to utilize Inotek's small molecule chemistry expertise as part of a multi-year collaborative research program and will pay for all future clinical development costs of INO-1001 and subsequent PARP inhibitors in cancer.

Also, Genentech has retained an option to develop and commercialize Inotek's PARP inhibitors to prevent cell death and complications associated with various acute cardiovascular conditions and procedures. The option is associated with an additional fee as well as development and other milestone payments. In total, the option, if exercised by Genentech, could be worth as much as $200 million in additional payments to Inotek if development, regulatory and net sales milestones are attained in multiple acute cardiovascular indications in various parts of the world. Inotek has retained an option to co-promote PARP inhibitors in the acute cardiovascular field in the United States with Genentech.

Inotek has retained all rights to develop and commercialize PARP inhibitors outside of cancer and the specific acute cardiovascular diseases included in Genentech's option.

* * *

Hologic Inc. (Nasdaq: HOLX) of Bedford, Mass., said it has completed the acquisition of **R2 Technology Inc**. of Sunnyvale, Calif., a producer of computer aided detection.

Under the agreement, the transaction purchase price is $220 million payable in 4,630,300 shares of common stock, the company said. The number of issued shares will be subject to reduction to reflect certain tax withholding obligations. Additionally, 10 percent of the shares will be held in escrow and subject to forfeiture to satisfy R2 stockholder indemnification obligations.

* * *

Infinity Pharmaceuticals Inc. of Cambridge, Mass., said **Amgen Inc.** has extended its non-exclusive access to the Infinity collection of natural product-like compounds for drug discovery.

Under the agreement, Amgen has the right to develop drug candidates it has identified from the compound collection, the company said. Infinity received an up-front license fee from Amgen and is eligible to receive milestones and royalties based on pre-clinical and clinical development and marketing of products resulting from its use of the compounds.

* * *

Receptor BioLogix Inc. of South San Francisco said it has acquired the cancer vaccine Insegia from Aphton Corp. of Philadelphia in a Chapter 11 bankruptcy sale approved by the U.S. Bankruptcy Court for the District of Delaware.

Insegia, also known as G17DT, has been studied for cancers of gastrointestinal origin, the company said. The immunotherapeutic stimulates production of antibodies that neutralize the peptide hormone, gastrin, a growth factor for GI malignancies, including stomach cancer and pancreatic cancer.

Two phase III trials of agent have been completed for advanced pancreatic cancer, and multiple phase II trials have been undertaken stomach cancer, which have shown promising results, the company said.

Insegia is generally safe and promising for GI cancers alone or in combination with chemotherapy, although further phase III testing is required to support regulatory approval, the company said.

* * *

Rosetta Genomics of North Brunswick, N.J., said it has secured the rights to patents covering hundreds of human microRNA sequences in diagnostic applications, through a co-exclusive license agreement with **Garching Innovation**, the technology transfer agency of the Max Planck Society, the company said.

In May, the company said it signed a microRNA licensing agreement with Rockefeller University, part of a broader strategy to expand its product development capabilities.

* * *

Tigris Pharmaceuticals Inc. Bonita Springs, Fla., said it has entered into an exclusive license agreement with NIH for the rights to commercially develop aminoflavone pro-drug, AFP-464, for cancer treatment.

AFP-464 is in two phase I trials sponsored by NCI for solid tumors, the company said. The mechanism of action of the pro-drug has shown it is converted to metabolites, which bind covalently to DNA, resulting in p53 activation and apoptosis. The pro-drug has shown a pattern of growth inhibitory activity in the NCI 60 tumor cell line screen, with breast, ovarian, lung and renal tumor cell lines exhibiting particular sensitivity to the compound.

Under the license, Tigris said it would provide the NIH development-based milestone payments and royalties based on sales of the licensed product.

In another development, **Tigris Pharmaceuticals Inc.** said it has entered into worldwide, exclusive license agreements with **H. Lee Moffitt Cancer Center & Research Institute**, **Yale University** and the **University of South Florida Research Foundation** for the rights to targeted cancer compounds.

Under the agreements, Tigris acquired the rights to small molecules, including GFB-204 and GGTI-2418. Tigris said it will pay development based milestones and royalties based on sales of the licensed products. Tigris said it would begin phase I trials for both GFB-204 and GGTI-2418 in 2007.