THE CANCER LETTER

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Klausner Resigns From Gates Foundation, Saying Move Unrelated To Investigation

By Kirsten Boyd Goldberg

Richard Klausner, executive director of the Global Health Program of the Bill and Melinda Gates Foundation, announced his resignation on Sept. 12, three days after The Cancer Letter reported the findings of a two-year Congressional investigation into potential conflicts of interest during his tenure as NCI director.

Klausner, who served as NCI director from 1995 to 2001, said in an email that his resignation had "absolutely no relationship whatsoever" to the investigation into NCI's award of a $40-million contract to Harvard University

(Continued to page 2)

In the Cancer Centers:

Three Centers Join Myeloma Consortium; Holden Wins NCI Renewal, 50% Increase

MULTIPLE MYELOMA RESEARCH CONSORTIUM said three cancer centers have joined the consortium: Emory University's Winship Cancer Institute, University of Chicago, and St. Vincent's Comprehensive Cancer Center of Saint Vincent Catholic Medical Centers of New York. The consortium brings together leading academic institutions to accelerate drug development in multiple myeloma and improve patient outcomes. "We are thrilled that these three institutions have joined the consortium," said **Kathy Giusti**, consortium founder and CEO. "By facilitating collaboration among these top academic cancer centers, we hope to spearhead drugs from the bench to the bedside as quickly as possible for patients with myeloma." Founding MMRC members include Dana Farber Cancer Institute, H. Lee Moffitt Cancer Center & Research Institute, Mayo Clinic Cancer Center, and University Health Network (Princess Margaret Hospital). Current research includes a pre-clinical effort to validate key targets in myeloma; a pre-clinical study, in collaboration with a biotech partner, to validate antibodies that may represent promising therapeutic options in myeloma; and a phase I trial and correlative sciences study in collaboration with Chiron Corp., of an FGFR3 inhibitor. . . . **HOLDEN COMPRENSIVE** Cancer Center at University of Iowa received a renewal of its NCI cancer center designation, said **George Weiner**, center director and C.E. Block Professor of Cancer Research. The renewal includes a five-year, $11.6 million P30 Cancer Center Support Grant, a 50-percent increase to more than $2.2 million per year. Holden recently opened a Center of Excellence in Image-Guided Radiation Therapy, Weiner said. . . . **MEMORIAL SLOAN-KETTERING CANCER CENTER** recent

(Continued to page 8)

Klausner: An "In-Box Rule" Covered Actions With Harvard

(Continued from page 1)

at the time Klausner was applying for jobs there.

Klausner will leave the Seattle-based foundation on Dec. 31 to start an undisclosed new venture.

Congressional investigators have asked the Government Accountability Office to audit NIH procedures that safeguard against conflicts of interest in contract awards (The Cancer Letter, Sept. 9).

Klausner said he believed that his actions in the Harvard contract were consistent with legal advice he was given by government ethics officials.

He said he was advised that the standard letters of recusal that he signed, disqualifying him from participating in "any matters affecting Harvard," only applied to making award decisions. In the case of the contract in question, the award decision followed the recommendation of a review committee.

"That was how I recall the advice we were given," Klausner wrote in an email to The Cancer Letter. "It was called the 'in-box rule' and related to action items 'in your in-box.' "

Klausner declined to elaborate. "I think, as the GAO is being asked to look at, not me or Harvard, but NIH policies about recusals, so I think all further info should come to The Cancer Letter from NIH," he wrote.

NIH officials declined to comment. "We can't speculate on Dr. Klausner's understanding of the terms of the recusal," said NIH spokesman John Burklow.

Multiple Actions Led To Harvard Contract

In August, the House Energy and Commerce Committee sent a 17-page letter to GAO describing evidence suggesting that Klausner participated "personally and substantially" in the development and award of the Harvard contract between 1999 and 2001, a period in which he was applying for at least two jobs there, including presidency of the university.

At that time, Klausner signed recusal letters that stated: "I have been advised that since I will be discussing job opportunities with Harvard University, I may not participate personally or substantially as a government employee in any matters affecting Harvard or any dealings they may have with the Federal Government."

However, the committee quoted emails and other evidence indicating that Klausner participated in a site visit to an NCI grantee at Harvard, Stuart Schreiber, to review progress and consider Schreiber's request for supplemental funding. According to the committee's letter, Klausner decided not to provide Schreiber with supplemental grant funding. Instead, apparently with Schreiber's participation, Klausner led NCI's development of a larger project, a "Molecular Target Laboratory," to be funded by a subcontract to Science Applications International Corp., the firm that has a contract for supporting cancer and AIDS research at NCI-Frederick.

Klausner authorized funding from the FY 2001 director's reserve for the MTL project, selected the NCI Source Selection Officer to oversee the review process, recruited members of the panel that reviewed the contract proposals, helped develop the evaluation factors used for scoring the proposals, and met with Schreiber several times to discuss the project, the committee's letter said.

After initially planning to fund at least two MTLs, Klausner was involved in a series of decisions to reduce the funding from $15 million to $8 million a year—enough money for only one lab, the committee's letter stated. Harvard's Schreiber was formally chosen to receive the five-year award in October 2001, just weeks after Klausner resigned from NCI.

The "In-Box Rule"

The "in-box rule" invoked by Klausner's email to The Cancer Letter appears to refer to a standard that HHS officials created specifically to allow Klausner

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to accept a $40,000 award from the University of Pittsburgh, sources said.

In a May 18, 2004, hearing, HHS ethics officers and officials from the Office of Government Ethics testified that Clinton Administration political appointees pressured ethics officers to allow Klausner to receive the university's 1997 Dickson Prize in Medicine and its cash award.

The NCI ethics officer and other ethics officials had recommended against Klausner receiving the money from the university, a major NCI grantee.

Edgar Swindell, associate general counsel of the HHS ethics division, testified that he was pressured to come up with a way to allow Klausner to accept the award. Swindell "wrote the legal opinion that interpreted the ethics regulations to allow an NIH official to receive a cash gift award from a grantee as long as there wasn't a pending matter in the official's in-box at the time the award was tendered," former Rep. James Greenwood (R-Penn.) said in his opening statement at the hearing last year.

"I am pleased that the Office of Government Ethics recognizes in its testimony for this hearing that the HHS interpretation was overly permissive," said Greenwood, who retired from Congress to become president of the Biotechnology Industry Organization. "Although the University of Pittsburgh insist that Dr. Klausner was selected on his merits, serious appearance questions are raised because of the timing and the circumstances of the award. In addition, it is amazing that the highest ranking ethics official at HHS ignored these appearance questions, disregarded OGE's advice, and may have provided a permissible but incorrect interpretation of ethics regulations to please political appointees."

Questioning Swindell, Rep. Diana DeGette (D-Colo.) commented on the in-box rule. "It seems to be a very, very nebulous standard," she said.

"That is a very good point, and that is the problem with it," Swindell agreed. "And that is why we are not going to operate under that and haven't operated under that kind of analysis about these questions."

The transcript of the hearing, "NIH Ethics Concerns: Consulting Arrangements and Outside Awards," is available at http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=108_house_hearings&docid=f:93973.wais.

"Change Is Good"

For the past three and a half years, Klausner has served as the top health officer overseeing programs in AIDS, tuberculosis, and malaria for the foundation begun by the Microsoft Corp. founder and his wife.

According to The Seattle Times, Klausner's salary was $435,887 when he was hired in 2002.

Klausner informed several colleagues at other organizations of his resignation in an email earlier this week. "Under the rubric of 'change is good', I wanted to let you know that last week I made the decision to step down as Executive Director of the Global Health Program of the Bill and Melinda Gates Foundation as of Jan 1, 2006," he wrote.

"The demands of travel and management and my desire to spend more time with family after a year of health challenges and personal change lead me to contemplate my work life and this has lead [sic] me to realize that it is the launching of new ventures and the creation of strategy that most excites and best suits me," Klausner wrote. "That realization, coupled with the incredible team that we have built here, makes this a good time for both me and the foundation to seek new leadership."

Klausner and his wife, Cecile Bassen, filed for divorce in July, The Seattle Times reported.

"I am pleased and excited about a new venture that I am about to lead that will allow me the great pleasure of staying in Seattle," Klausner's email continued. "I and my partners in this new venture will soon be announcing our plans."

A Gates Foundation spokesman said the announcement followed months of discussion between Klausner and Patty Stonesifer, foundation president and co-chairman. The two decided that the program needed new leadership, said Jacquelline Fuller, a spokesman for the foundation. "The foundation's view is that Dr. Klausner's contribution to developing strategy for the Global Health Program was invaluable to the program and will be continued," Fuller said.

Paul Goldberg contributed to this report.

FDA News:

ODAC Approves Tarceva For Pancreatic Cancer

By Paul Goldberg

The FDA Oncologic Drugs Advisory Committee voted for approval of Tarceva (erlotinib) in combination with gemcitabine for advanced pancreatic cancer in patients who have not received chemotherapy.

Voting for approval of the oral drug sponsored by OSI Pharmaceuticals Inc. and Genentech Inc., ODAC accepted that the modest survival advantage—about two weeks, according to FDA—was convincingly

demonstrated in a phase III trial and constituted a clinical benefit to patients.

Also, at the meeting Sept. 13 and 14, ODAC made the following recommendations:

—The committee voted unanimously against approval of Abbott's Xinlay (atrasentan) for hormone-refractory prostate cancer that has spread to the bone. The pivotal phase III trial failed to meet primary and secondary endpoints and was halted by the data and safety monitoring board. However, the company filed an application for approval based on a post-hoc analysis of a subset of patients.

—The Celgene Corp. drug Revlimid (lenalidomide) was recommended for full approval for the treatment of transfusion-dependent anemia due to low- or intermediate-1 risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.

Several members of the committee said they were concerned about the drug's toxicity at the dose studied in phase II registration trial and feared that the approval may hamper ongoing phase III trials comparing the drug's doses.

—Arranon (nelarabine), sponsored by GlaxoSmithKline (NYSE: GSK) was recommended for accelerated approval for T-cell acute lymphoblastic leukemia and T-cell lymphoblastic lymphoma in pediatric and adult patients whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens.

The drug was kept alive for decades through persistence of several investigators, cooperative groups and NCI, sources said.

Committee Instructed To Ignore Cost of Tarceva

"We are not supposed to be bringing into consideration financial concerns about drug pricing," Richard Pazdur, director of the FDA Office of Oncology Drug Products, said to the committee. "That is a separate issue from a regulatory decision that is being made here. I want to emphasize that the decision regarding this drug should be made on the basis of safety and efficacy that is presented to you, not on any cost consideration, how much the drug may cost, what is the [cost and] benefit per patient by year, by month, or by day? That is a non-FDA question that should not, and must not impact on a decision regarding the approval or non-approval of the drug."

The regimen recommended in the Tarceva supplemental New Drug Application costs about $2,084 a month on the retail level. Tarceva, an epidermal growth factor receptor inhibitor, is approved for non-small cell lung cancer for patients whose disease progressed after one or more courses of chemotherapy.

It is unclear why the agent appears to work with gemcitabine in pancreatic cancer when earlier combinations of EGFR inhibitors with chemotherapy for lung cancer were unsuccessful, Pazdur noted. Also, scientists are yet to find the tools for identifying patients who stand to benefit from either Tarceva or its sister drug Iressa.

The ODAC recommendation suggests that with aggressive diseases like pancreatic cancer, even a barely visible survival benefit pinpointed in a randomized trial can lead to an approval.

FDA's Pazdur urged the committee to refrain from getting bogged down in trying to pinpoint an acceptable minimal duration of an improvement.

"One point that deserves some discussion is how much survival constitutes a clinical benefit," Pazdur said. "That is a very difficult question for anyone… To say that X amount of days is a benefit, and X-2 days is not a benefit, might not be the most appropriate question to be had here. The question here is, do we truly have a true finding, and, then, is it a clinical benefit in terms of the toxicity?"

Possible interstitial lung disease was experienced in 2.3 percent of patients in the Tarceva plus gemcitabine arm compared with 0.4 percent in the gemcitabine plus placebo arm, the company said.

The incidence of serious ILD-like events in the Tarceva and gemcitabine arm was higher than the 0.8 percent incidence reported for both the Tarceva monotherapy and placebo arms in the Tarceva pivotal study in advanced NSCLC. The incidence of possible ILD from all clinical studies with Tarceva is 0.7 percent, the company said.

According to the company, rash was the most common adverse event associated with Tarceva in this indication. It was reported in 69 percent of patients who received Tarceva plus gemcitabine and in 30 percent of patients who received gemcitabine plus placebo.

Diarrhea was reported in 48 percent of patients who received Tarceva plus gemcitabine and in 36 percent of patients who received gemcitabine plus placebo, the company said.

Two percent of the patients discontinued Tarceva because of a rash and two percent because of diarrhea.

ODAC chairman Silvana Martino, of the University of Southern California Keck School of Medicine, said she was unimpressed by the company's exploratory study of the quality of life.

"The group that received Tarceva didn't do any better or any worse," Martino said. "There was a little more diarrhea, a little bit more rash. If I were to summarize all that, I would say, 'Gee, maybe I would live a little longer, but from the clinical perspective, other than counting whatever days those are, and I am still uncertain what those days are… The very fact that I have to use the word 'days' still bothers the hell out of me, by the way, for all of you, including Dr. Pazdur. But if all I am going to do during those days is have a rash and diarrhea, it bothers me that the quality of life was not made better by something that prolongs my survival.' "

Responding to Martino, Mace Rothenberg, Ingram Professor of Cancer Research at Vanderbilt Ingram Cancer Center, said Tarceva's toxicity is milder than that of many GI cancer drugs.

"The incidence of Grade 3 or 4 diarrhea in this trial with Tarceva was less than 6 percent," said Rothenberg, a consultant to the company. "Compared to other drugs I have worked with before and presented to ODAC, that's quite a bit less. In addition, when you look at the incidence of severe toxicities, that's toxicity that could occur at any point along the treatment time. So when you talk about that additional life gained by the drug being tainted by this toxicity, that actually may not be the case. The toxicity may have occurred early, been addressed adequately, and that patient may have enjoyed a good quality of life."

A phase III trial of Tarceva and gemcitabine met its primary endpoint of improving survival. The trial randomized 569 patients to receive gemcitabine plus concurrent Tarceva or gemcitabine and placebo. Altogether, 521 patients were randomized to receive 100 mg/day of Tarceva or placebo, and 48 patients were randomized to receive 150 mg/day of Tarceva or placebo.

The ODAC review focused on the cohort that received the 100mg per day dose.

Patients receiving gemcitabine plus Tarceva demonstrated a statistically significant (23 percent) improvement in overall survival (hazard ratio = 0.81, p = 0.028), which can also be referred to as a 19 percent reduction in the risk of death, the company said.

After a year, 23 percent of patients receiving Tarceva plus gemcitabine were alive compared to 17 percent of patients receiving gemcitabine plus placebo, the company said.

A statistically significant improvement in progression-free survival (hazard ratio = 0.77; p = 0.006) was also demonstrated. Although no difference in tumor response was observed (8.6 percent in patients receiving Tarceva plus gemcitabine versus 7.9 percent in the gemcitabine plus placebo arm), the disease control rate (complete response + partial response + stable disease) was significantly improved (59 percent in patients receiving Tarceva plus gemcitabine versus 49 percent in the gemcitabine plus placebo arm, p = 0.036).

Roche, OSI's European partner, is conducting a study of Tarceva and gemcitabine vs. Tarceva, gemcitabine plus Avastin.

OSI said an application of the proportional hazard ratio to survival would translate to a five-week improvement in median survival.

"I think if you work in a field of pancreatic cancer, most of the time you expect trials to be negative, because that's the usual result, and, obviously, I wish this were adjuvant Herceptin in breast cancer, but it isn't," said Malcolm Moore, the principal investigator on the study, professor of medicine and pharmacology at the University of Toronto Princess Margaret Hospital and chair of the GI committee of the NCIC Clinical Trials Group.

"I guess the question is, when you have a horrible disease like pancreatic cancer, where the median survival is only six months, the absolute improvement of a hazard ratio of 25 percent is only one to two months," Moore said at ODAC. "So it's a question of do we penalize people who have these very aggressive diseases by saying we are going to require a higher standard in terms of survival than we apply to other diseases."

ODAC member Maha Hussain said it would be unfair to apply higher standards for approval of new generation drugs like Tarceva. Though these drugs are believed to hit specific targets, their mechanism of action and the principles for selection of patients likely to benefit from therapy remain uncertain.

"The clinical application of the use of a drug can go much faster than the preclinical work," said Hussain, an oncologist at the University of Michigan. "Even with chemotherapy, where we think we know how it works, we still don't know why patients respond and don't respond, and in the last 60 years we haven't figured it out. I don't think that we ought to hold clinical trials hostage to the mechanism issue."

The committee voted 10-3 in favor of approval.

Xinlay and The Question of Post-Hoc Analysis

Abbot's drug Xinlay (altrasentan) had some strikes against it: the pivotal trial was stopped after an independent data and safety monitoring board determined that it would be futile to continue.

The study, which compared Xinlay with placebo in 809 patients with hormone-refractory prostate cancer, failed to meet its primary endpoint, time to disease progression. Also, the trial failed to meet four out of five secondary endpoints and many of its tertiary endpoints.

Only one secondary endpoint was met—mean change in bone alkaline phosphatase—but the agency questioned its clinical relevance.

Other problems included deaths from cardiovascular events in the treatment arm, and the agency's determination that the company's confirmatory trial was unacceptable. Also, the agency recently approved docetaxel for the same patient population. That approval was based on a demonstrated survival advantage.

These problems notwithstanding, Abbot conducted several subgroup analyses that were not specified in the protocol, and asked for a regular approval for a subgroup of patients who had bony metastases, but were asymptomatic. The NDA supplied data on time to disease progression and delay in time to onset of bone pain.

The committee voted 13-0, against approval, in effect upholding the fundamental principles that a post-hoc subset analysis of a negative trial cannot be described as statistically convincing, and that a finding that is not statistically persuasive cannot be relevant in the clinic.

"I think I have in the past, in this very committee, become red-faced, arguing over and over again that you really shouldn't talk about clinical significance if you don't have statistical significance," said Ralph D'Agostino, professor of mathematics and statistics at Boston University Mathematics Department, a voting consultant to ODAC. "I think that's a very important scientific step."

"The finding is not statistically significant. Therefore, any numbers that we get are a fluke," agreed Otis Brawley, professor of medicine, oncology and epidemiology at Emory University School of Medicine and a consultant to ODAC.

Several members of the committee said the company's data suggests that Xinlay has activity, and many said they were reluctant to vote against approval. "I have hope for this drug, but I think that approval at this time, based on the current application, is premature," Brawley said. "I take care of prostate cancer patients, and I would like to see prostate cancer patients have options. However, I would want them to have legitimate options. I keep pictures in my office of patients who have been harmed by illegitimate options in therapy. Development of this drug would be slowed down if we were to approve it at this time."

Xinlay is an investigational, oral, once-daily, non-hormonal, non- chemotherapy, agent that belongs to a class of compounds known as selective endothelin-A receptor antagonists (SERA). SERAs antagonize the effect of endothelin-l (ET-l), one of the proteins thought to be involved in the stimulation of the growth and spread of cancer cells.

"Abbott respects the committee's vote on Xinlay today; however, we continue to believe that Xinlay represents an important option for patients with advanced prostate cancer who currently have limited options," Eugene Sun, Abbott vice president, Global Pharmaceutical Clinical Development, said in a statement. "The company is encouraged by committee member statements regarding the activity of Xinlay and the value of continuing development of the drug. We await FDA's decision on Xinlay."

The agent is being studied in earlier stage prostate cancer patients in an ongoing phase III study in hormone-refractory prostate cancer patients without metastasis, the company said.

The study to expected to be completed in 2006.

Revilmid Recommended Based on Phase II Data

FDA officials said they had advised Celgene to conduct a randomized trial would be needed to evaluate Revilmid. However, the company filed an NDA based on a single-arm trial that demonstrated strong efficacy in MDS.

The agency asked ODAC whether it was possible to separate Revilmid's treatment effect from statistical noise and weigh the drug's benefits against its considerable toxicity.

In the open label pivotal phase II trial that enrolled 148 patients, approximately two-thirds of patients achieved resolution of chronic refractory anemia resulting in transfusion independence, the company said.

Response was associated with meaningful cytogenetic and bone marrow remission, and responder median hemoglobin increased more than 5.0 grams per deciliter, the company said. After median follow-up of 58 weeks, the median duration of transfusion-independence response had not yet been reached, the company said.

About 80 percent of patients couldn't tolerate the treatment at the induction dose of 10 mg and had to have dose reductions to 5mg. The major side effects leading

to dose reductions were cytopenias.

In an integrated summary of three trials that altogether enrolled 408 patients, 28 died while on study and additional 14 deaths were attributed to continuing toxicity, the agency said.

"There is clear evidence for a signal at some level," said Thomas Fleming, a biostatistician at the University of Washington School of Public Health and Community Medicine and consulting member of the committee. "It's also very apparent through the nature of sampling and issues of bias that we certainly cannot attribute the entirety of this response to treatment effect.

"There certainly is noise, and there is certainly bias in the way it is being assessed," Fleming said. "Does this trial provide substantial evidence for some level of benefit? … Yes. But everything is benefit-to-risk, and if the safety profile is pristine, then that answer is probably adequate.

"But the safety profile is not necessarily pristine--and difficult to understand," Flemingh said. "Do we have reliable evidence to allow us to assess benefit to risk in a conclusive fashion? So if there is, in fact, a substantial risk, can we reliably indicate what is the level of benefit? I am struck by the almost complete absence of an indication of what an appropriate comparator arm would do on these key measures that we are asked to look at for efficacy."

ODAC member Bruce Cheson, head of hematology at Georgetown University's Lombardi Comprehensive Cancer Center, concurred with Fleming's assessment.

"I am convinced there is activity here, but I am very worried," he said at the meeting. "What we heard is that the [investigators] in this clinical trial can't tell if cytopenias are related to the drug or the disease with any sort of reliability. The majority of deaths on this trial were not attributed by the investigators to the drug, but on a secondary independent review, were identified as drug-related deaths. So, physicians in the community have difficulty not only identifying toxicities, but also when the drug is potentially lethal, and here we have a dose, which 80 percent of the people cannot tolerate.

"We don't know that 5mg will not give us the exact same effect, and we are told that we will put this on the street, and leave it up to [community oncologists] to modify the dose accordingly when couldn't even modify it, appropriately during the conduct of a clinical trial," Cheson said.

"Whereas I would love to see this drug on the market, because it would benefit some patients, I think the dose is an unsafe dose, I think the schedule is difficult for most practicing oncologists in a busy practice to manage."

However, the majority of the committee agreed with the views Susan O'Brien, a professor of Medicine at the M.D. Anderson Cancer Center's Department of Leukemia, that the drug's activity is formidable and toxicity manageable.

"Adjusting drugs because of myelosuppression is not rocket science," said O'Brien, a consulting member of the committee. "Everybody in oncology does it. It's not very hard to do. I am so struck by the efficacy—and I do think that this is a toxicity that is not that difficult to deal with--that I think that it's much more important to get the drug out."

The committee voted 10-5 for approval.

Revlimid is a member of a new class of novel immunomodulatory drugs. Celgene is evaluating the agent for multiple myeloma, MDS, chronic lymphocytic leukemia as well as solid tumors.

Arranon Accelerated Approval Recommended

ODAC voted unanimously for an accelerated approval of Arranon for adults and 11-1 for an accelerated approval in pediatrics.

The committee reviewed data from two, multi-center pivotal phase II clinical trials evaluating a total of 39 adults and 151 children with T-ALL or T-LBL. The trials were conducted by cooperative groups under the sponsorship of the NCI.

The efficacy data to support the proposed indication focuses on 28 adults and 39 children that had multiple relapses following, or were refractory to, at least two prior induction regimens, the company said.

Key efficacy results showed that 21 percent of the adults and 23 percent of the children achieved a complete response or a complete response without full hematological recovery with single agent Arranon.

A majority of those were CRs (18 percent in adults and 13 percent in pediatric patients), the company said. Remissions were considered durable and generally long enough to allow for stem cell transplant procedure, often the intent following successful induction of remission.

Following Arranon, patients had a median overall survival of 21 weeks for adults and 13 weeks for children and one-year survival rates of 29 percent in adults and 14 percent in children.

Hematologic toxicity was the most common NCI Common Toxicity Criteria Grade 3 or 4 adverse event in the studies, the company said. Consistent with other cytotoxic agents, Arranon is associated with neurological events, some considered severe.

The compound was discovered in the 1960s by

Gertrude Elion, a Nobel laureate and a researcher at Burroughs-Wellcome. It is a water-soluble prodrug of ara-G with T-cell selectivity, the company said.

In 1981, Elion gave the drug to Joanne Kurtzberg, now director of Duke University's pediatric stem cell transplant program. In the nineties, Kurtzberg conducted phase I studies of the agent, and other researchers and cooperative groups launched subsequent studies.

As the studies were conducted, NCI's CTEP handled the drug's distribution. Throughout the development of the compound, more than 980 patients have been treated, the company said.

Meanwhile, Burroughs-Wellcome became part of Glaxo, and, later, GlaxoSmithKline, the company that filed the NDA for the drug. The application was based on studies conducted by the Children's Oncology Group and the Cancer and Leukemia Group B, in conjunction with the Southwest Oncology Group.

"There simply aren't many options currently available for these treatment-resistant cancers, especially in children, therefore ODAC's recommendation is very encouraging," Richard Larson, director of the Hematologic Malignancies Program at the University of Chicago and the CALGB Leukemia Committee chairman said in a statement.

In the Cancer Centers:

MSKCC's Varmus Elected To Royal Society of U.K.

(Continued from page 1)

appointments and awards: MSKCC President **Harold Varmus** was elected a foreign member of the Royal Society, the U.K. national academy of science. **James Allison,** chairman of the Immunology Program, received the 2005 William B. Coley Award for Distinguished Research. **Carol Aghajanian** was named chief of the renamed Gynecologic Medical Oncology Service in the Department of Medicine. She had been acting chief since 2004, when the service was known as the Developmental Chemotherapy Service. **David Kissane**, chairman of the Department of Psychiatry and Behavioral Sciences, was named to an Alfred P. Sloan Chair. **Pier Paolo Pandolfi** is the first incumbent of the Albert C. Foster Chair. Pandolfi, a cancer geneticist, is head of the Molecular and Developmental Biology Laboratory. **Gavril Pasternak**, head of the Molecular Neuro-Pharmacology Laboratory, was named to the Anne Burnett Tandy Chair of Neurology. **John Petrini**, head of the Laboratory of Chromosome Biology, is the incumbent of the Paul G. Marks Chair in Molecular Cell Biology. **Roger Wilson**, chairman of the Department of Anesthesiology and Critical Care Medicine, was named to the Founder Chair. **Vera Safai** was elected president of the Society of MSKCC. . . **OHIO STATE** University Comprehensive Cancer Center and Cincinnati Children's Hospital Medical Center, a teaching affiliate of the University of Cincinnati College of Medicine, have formed a research collaboration in gene therapy and cell treatment in pediatric cancers. Also, the center appointed **Vipul Patel** clinical associate professor of surgery and director of the fellowship program in minimally invasive urologic surgery. Two Ohio State faculty, **John Byrd** and **D. Warren Brown**, received a five-year Specialized Center of Research, $6.25 million grant from the Leukemia & Lymphoma Society for chronic lymphocytic leukemia research. Byrd is a hematologist/oncologist and Brown is professor of leukemia research. The grant will fund four research projects and three clinical trials. Project leaders include **Michael Grever**, **Michael Freitas**, and **Ching-Shih Chen**. . . . **ROSWELL PARK** Cancer Institute held a celebration of the 25th anniversary of the PSA test, discovered at Roswell Park by **T. Ming Chu**. **Donald Coffey**, of Johns Hopkins University School of Medicine, presented the T. Ming Chu Distinguished Lecture, "The Continuing Impact of Progress in Urology Stemming from Early Discoveries at Roswell Park."

A Notch-Signaling Pathway Inhibitor in Patients with T-cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL)

An investigational study for children, adolescents and adults with relapsed and refractory T-cell acute lymphoblastic leukemia/lymphoma is now accruing patients at various centers around the country.

This study's goal is to evaluate the safety and tolerability of a Notch inhibitor as a rational molecular therapeutic target in T-ALL, potentially uncovering a novel treatment for these cancer patients.

Eligibility criteria and treatment schema for the study include:

Notch-Signaling Pathway Inhibitor in Patients with T-ALL	
Eligibility Criteria	Patient must be = 12 months with a diagnosis of T-cell acute lymphoblastic leukemia/lymphoma AND must also have: • Relapsed T-ALL • T-ALL refractory to standard therapy • Not be a candidate for myelosuppressive chemotherapy due to age or comorbid disease ECOG performance status =2 for patients >16 years of age OR Lanksy performance level >50 for patients 12 months to =16 years of age Fully recovered from any chemotherapy and >2 weeks from radiotherapy, immunotherapy, or systemic steroid therapy with the exception of hydroxyurea or intrathecal therapy Patient must be >2 months following bone marrow or peripheral blood stem cell transplantation No treatment with any investigational therapy during the preceding 30 days No active or uncontrolled infection
Treatment Plan	Open label and non-randomized, this study is conducted in two parts. Part I is an accelerated dose escalation to determine the maximum tolerated dose (MTD), and Part II is a cohort expansion at or below the MTD. MK-0752 will be administered orally. Plasma concentrations will be measured at defined time intervals.

For information regarding centers currently open for enrollment, please contact 1-888-577-8839.

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