THE CANCER LETTER

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ODAC Votes 9-6 In Favor of Clolar For ALL, Doesn't Recommend Marqibo For NHL

By Paul Goldberg

An FDA advisory committee voted 9-6 to recommend approval for Clolar (clofarabine) for refractory or relapsed pediatric acute lymphoblastic leukemia.

Though the sponsor, Ilex Products Inc., sought approval for the broader indication of pediatric refractory or relapsed acute leukemia, ODAC supported the drug's use for ALL, but not for acute myeloid leukemia.

Separately, ODAC voted down Marqibo (vincristine sulfite liposome injection) for aggressive non-Hodgkin's lymphoma previously treated with at

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In Brief:

CCRI Recruits Faculty; Two Center Directors Named: Kastan At St. Jude, Willson At Simmons

CHILDREN'S CANCER RESEARCH INSTITUTE at the University of Texas Health Science Center at San Antonio announced faculty recruitment, said **Sharon Murphy**, the institute's founding director. **Alex Bishop** joined the CCRI as a principal investigator in molecular oncogenesis. He received his doctoral degree from Oxford University and completed two postdoctoral fellowships at Harvard University. **Charles Keller** will begin his appointment in January as a principal investigator in developmental cancer genetics and therapeutics. Keller received his medical degree from Baylor College of Medicine, completed his internship and residency in pediatrics at Texas Children's Hospital, and trained in pediatric hematology-oncology at the University of Utah. **Donald McEwen**, also will join the CCRI in January as a principal investigator in molecular oncogenesis. McEwen received his doctoral degree from Washington University and completed his postdoctoral fellowship at the Lineberger Comprehensive Cancer Center at the University of North Carolina. . . . **MICHAEL KASTAN** was named director of the St. Jude Cancer Center at St. Jude Children's Research Hospital. He will serve as principal investigator of the NCI Cancer Center Support Grant and will continue as chairman of hematology-oncology and chairman of the Cancer Center Advisory Committee. **James Downing** was named scientific director at St. Jude. He replaces **William Evans**, who was named director of the hospital earlier this month. Downing will continue as chairman of pathology. . . . **JAMES WILLSON,** director of the Ireland Cancer Center in Cleveland, has been named director of the Harold C. Simmons Comprehensive Cancer Center at UT Southwestern Medical Center at Dallas. Willson also was named the

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The Cancer Letter Takes Winter Break

This is the final issue of **The Cancer Letter** for 2004. The next issue, Vol. 31 No. 1, is scheduled for publication on Jan. 7, 2005. **The Cancer Letter** is published 46 times a year.

ODAC Upholds Durable CRs As Endpoint For Leukemias

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least two chemotherapy regimens. Marqibo is sponsored by Inex Pharmaceuticals Inc., a Canadian firm.

In remarks that opened the two presentations, Richard Pazdur, director of the FDA Division of Oncology Drug Products, asked ODAC for guidance on using the accelerated approval mechanism in a systematic manner, and the committee seemed eager to oblige:

--In both applications, ODAC upheld the conventional endpoint of durable complete remission for hematologic malignancies, rejecting alternative endpoints of complete remission without platelet recovery, partial remission, or ability to go to transplant as evidence of clinical benefit needed to support approval.

--In the Marqibo application, the committee concluded that, based on medical literature, patients with lymphoma have a number of treatment options known to produce substantial response rates, which makes it difficult to determine whether an experimental therapy is indeed a treatment of last resort.

The 1992 law that established the accelerated approval mechanism requires that treatments represent an improvement over existing therapy for the indication in order to be approved based on a surrogate endpoint likely to suggest clinical benefit. This guidance by the committee likely means that sponsors of lymphoma treatments would need to demonstrate superiority of the safety or efficacy of new therapies in randomized trials.

In recent years, FDA struggled to find an approach to granting accelerating approvals in a meaningful, systematic manner. However, once the data from single-arm trials got to ODAC, some committee members took it as an invitation to give the benefit of the doubt to drugs supported by muddled data or to find a way to get drugs on the market solely on the basis of their biological activity.

Before posing the approval question on Marqibo, committee member Sylvana Martino urged her colleagues to base their votes exclusively on the data presented that day.

"Can I just make it very simple?" said Martino, a breast cancer expert at Cancer Institute Medical Group of Santa Monica, Calif., who served as chairman at the presentation. "What the question is about is, from what we have heard today, do you believe that there is enough substantial data to give approval for this drug so it is available for someone to use tomorrow? We cannot confuse the issue of, is there any activity, is there any value? It's not the minimum requirement here. That cannot be our goal here. If it is, I am done with this group as of this moment."

The committee voted unanimously against approval.

Even with Clolar, the ODAC vote doesn't guarantee approval, sources said. The agency is more likely to be influenced by a majority vote, and even then a clear post-approval strategy would be required. No post-approval plans have been presented by Ilex, FDA officials said at the meeting, although this is a disputed assertion.

Also, the Clolar recommendation applies to a pediatric cancer, a scientific environment where physicians are accustomed to making do with small studies and, at times, extrapolation from adult data.

Establishing what may be a new ODAC policy, committee member Otis Brawley asked scientists presenting for the sponsors to disclose their commercial interest in the products.

Financial involvement of presenters is disclosed to FDA, but the agency hasn't made this information public in a systematic manner.

Brawley's point-blank question forced an acknowledgement by Fernando Cabanillas, medical director at Auxilio Cancer Center in Puerto Rico, that he and his former institution, M.D. Anderson Cancer

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

Editorial: 202-362-1809 Fax: 202-318-4030
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Center, hold a use patent for Marqibo.

Cabanillas was the principal presenter for Inex, and the drug was tested at M.D. Anderson. At the meeting, Pazdur acknowledged that FDA was informed about this involvement, but said that the agency saw no evidence of impropriety in either informed consent or the conduct of the trial.

Pazdur's introductory remarks at the Clolar and Marqibo presentations appear to reflect the agency's cumulative experience and its strategy for implementation of the accelerated approval regulations.

The text of his remarks appears below.

On Clolar (clofarabine):

The sponsor of the application in this morning's session requests marketing approval of clofarabine for the proposed indication of the treatment of pediatric patients with refractory or relapsed acute leukemia.

The presentations will focus on one single-arm trial conducted in 35 patients with relapsed/refractory AML and a second single-arm trial in 49 patients with relapsed/refractory ALL. A phase I study was also conducted in 25 patients with relapsed/refractory acute leukemia.

For the treatment of acute leukemia, the division has recommended the use of improved survival or a complete response rate of a sufficient magnitude and duration to ensure the demonstration of clinical benefit.

Complete response rates of sufficient duration are considered clinical benefit because they are usually associated with reductions in infection rates and blood transfusions and may be considered established surrogates for survival in this disease.

Response duration is usually measured from the time of initial response until documented tumor progression. One problem encountered in this application is the introduction of bone marrow transplantation in patients who have received clofarabine, but have not had documented disease progression. The addition of transplantation prior to the documentation of disease progression confounds any interpretation of clofarabine's response duration.

No consistent, prospective criteria were used to determine patient selection for transplantation. Some patients went to transplantation with only a clofarabine partial response or even without a response in these single-arm trials. A clofarabine induction response may simply indicate a chemosensitive leukemia and the patient might do as well with transplantation without clofarabine induction.

In patients who did not go on to transplantation, and, hence, response duration can be measured, these response durations were generally short and many of these responses were of uncertain duration because they were not confirmed by a repeat marrow aspirate.

These results are presented in the preamble to your ODAC questions. In the 35 patients with AML, there were no complete responses, only one complete response without complete platelet recovery (CRp), and eight partial responses. Of these nine responding patients, two patients did not go to transplantation prior to disease progression. These patients all had PRs. Their response durations were short: 12, 34 days.

Of the 49 patients with ALL, there were 6 CRs, 4 CRps, and 5 PRs. In this population, response duration was not confounded by transplantation in only nine patients. The five patients with CRs had response durations of 43, 50, 82, 93+, and 160+days. Only three of these five CRs had a confirmed response. As in AML, PRs had very short response durations of only seven, 16, and 21 days.

As stated previously, the agency has recommended a substantial complete response rate and duration as endpoints for regular approval in hematological malignancies denoting direct clinical benefit.

In 1992, the accelerated approval regulations allowed the use of additional endpoints for approval of drugs that are intended to treat serious and life-threatening disease and that either demonstrate improvement over available therapy or provide therapy where none exits. The FDA may grant accelerated approval based on the effect of a surrogate endpoint that is "reasonably likely" to predict clinical benefit.

A drug is approved under accelerated approval rule on the condition that the manufacturer conduct studies to verify and describe the clinical benefit. The regulations stated an expectation that post-marketing studies would usually be underway prior to accelerated approval, but this is not a requirement.

At a March 2003, ODAC meeting, the ODAC reinforced the agency's view that these confirmatory trials should be ongoing at the time of accelerated approval is granted. Approval with the subsequent commercial availability of the drug may interfere with subsequent enrollment to the confirmatory trial.

We are asking your opinion regarding accelerated approval of clofarabine based on the data presented. The ALL indication should be considered separately from AML. There exists uncertainty regarding the response duration because of the lack of subsequent bone marrow biopsies to confirm a response and the introduction of transplantation prior to documentation of disease progression.

Where duration can be measured, the division considers—with some exceptions—these response durations to be limited. We have asked the sponsor to present current ongoing and planned trials in both pediatric and adult leukemia. Presently, we have not identified any study that has been designated as a confirmatory trial for the subsequent demonstration of clofarabine clinical benefit.

For our division, this is the first time we are considering a pediatric application for accelerated approval. Pediatric drug development and the treatment of pediatric malignancies differs from adult drug development. Therefore, we have supplemented this ODAC membership with voting members from the pediatric oncology community.

Pediatric drug development trials have been blessed by

exceptionally high patient enrollment compared to enrollment in adult studies. Great strides have been made in curing and prolonging the survival of children in the past decades. Most children—especially with the diseases under consideration this morning—are treated on protocols at referral centers rather than in the community.

Your discussions should consider the ramifications of accelerated approval for the pediatric development of clofarabine. Approval of the drug for a pediatric oncology indication should not be at a lesser standard than that expected for an adult indication.

Approval decisions should be based on a risk-benefit determination. A reasonable question is whether the necessary information regarding this risk benefit relationship can be derived from a single-arm study where the primary endpoint is confounded by the introduction of a subsequent therapy—bone marrow transplantation.

Your decision regarding the approval status of this drug should be based on the above scientific decision, not simply a desire to provide drug access to patients. Access to a yet to be approved drug—especially, with limited patient populations encountered in these indications—can be accomplished through additional registration trials and expanded access programs.

We are interested in your discussions on the impact of this drug's accelerated approval at this time and timely completion of any confirmatory trials in pediatric oncology.

An appropriate question is whether drug approval at this time, especially since a designated confirmatory trial is not underway, may interfere with the conduct and completion of confirmatory trials.

Discussions may focus on whether approval of this drug with its response rate and the uncertainties regarding response duration is appropriate or whether additional data should be available before a definitive approval decision is made.

On Marqibo (vincristine sulfate liposome injection):

This afternoon's session focuses on the marketing application of vincristine sulfate liposomes for the treatment of patients with aggressive, relapsed non-Hodgkin's lymphoma treated with at least two combination chemotherapy regimens. The sponsor is seeking accelerated approval for this agent.

Since there are members of the committee who did not attend this morning's session, I would like to reiterate several comments made earlier regarding accelerated approval and then comment on issues specific to this application.

The demonstration of clinical benefit is required to achieve full approval. In oncology, the demonstration of clinical benefit has usually been an improvement in overall survival or an amelioration of disease-related symptoms.

In 1992, the accelerated approval regulations allowed the use of additional endpoints for approval of drugs that are intended to treat serious and life-threatening diseases. These drugs may either demonstrate an advantage over available therapy or provide therapy where none exists. The FDA may grant accelerated approval based on the effect of a surrogate endpoint that is "reasonably like" to predict clinical benefit.

A drug is approved under the accelerated approval rule on the condition that the manufacturer conduct studies to verify and describe the clinical benefit. The regulations stated an expectation that post-marketing studies would usually be underway prior to accelerated approval, but this is not a requirement.

At a March, 2003 ODAC meeting, the ODAC reinforced the agency's view that these confirmatory trials should be ongoing at the time accelerated approval is granted. Approval with the subsequent commercial availability of the drug may interfere with the enrollment to the confirmatory trial.

Accelerated approval has been based on an objective response rate with adequate duration in single-arm studies in patients with refractory disease.

Since an agent must demonstrate an advantage over available therapies or provide therapy where none exists, we are asking you to consider if available therapy exists for the indication under consideration. If effective available therapy exists, a randomized trial comparing the investigational drug to an available therapy arm would generally be needed to demonstrate superiority.

Available therapy usually consists of drugs that are indicated in drug labeling for the treatment of a specific disease. However, in oncology where drugs are frequently used in non-approved indications as single agents or in combinations, available therapy may constitute therapy substantiated by "compelling" literature evidence of efficacy. There is no regulatory definition of the word "compelling"—hence, we are asking your opinion.

We are not asking you to reach a consensus on a specific therapy. Available therapy may be a single drug or may be a combination regimen. Available therapy may be several regimens or drugs. Where there may be lack of consensus regarding a single specific treatment, the agency has even recommended using several regimens or drug as a treatment arm with the stipulation that superiority is demonstrated by the investigational agent.

The primary endpoint of this single-arm trial is response rate. The interpretation of a response rate is complex. We have emphasized that the persuasiveness of the results of a single-arm trial to support accelerated approval hinges on the magnitude and duration of the responses observed in trials.

In aggressive lymphomas, we have emphasized to sponsors the importance of complete response rates of adequate and well-defined duration as an endpoint for drug approval. In selected hematological malignancies where partial responses are observed, we have been impressed with substantial response durations and these have led to approval. For example, the recently approved Velcade for the treatment of refractory multiple myeloma had a median response duration in excess of one year. Similarly, the median duration of disease control for fludarabine in CLL was in excess of one year.

Since the vast majority of responses noted in this

application are partial responses with uncertain durations—13 out of the 30 responders did not even have a single repeat scan or progressed before a repeat scan could be performed—we are asking your opinion regarding of this endpoint. Remember, this endpoint in this study must be "reasonably likely" to predict clinical benefit.

In the morning session, we highlighted the need for confirmatory trials to be ongoing at the time of drug approval. This is not a requirement, however, the ODAC has supported our viewpoint that accelerated approval trials be part of a comprehensive drug development plan with early initiation of confirmatory trials prior to drug approval.

To date, a confirmatory trial for VSLI has neither been started nor agreed upon with the FDA. In your deliberations, discussion must focus on this aspect and the impact that any approval would have on the conduct and completion of any confirmatory trial.

I would like to emphasize that the accelerated approval process is not simply a screening process for drug activity. Mere demonstration of nominal activity is insufficient for accelerated approval.

Response rates must provide convincing evidence that the magnitude and duration of responses are reasonably likely to predict clinical benefit. This response rate and duration may vary from one disease to another.

The accepted response rate in refractory metastatic colon cancer may have little bearing on that accepted for refractory aggressive lymphoma. Hence, we are asking for your clinical judgment in this disease setting. There must be confidence in any recommendation that a drug approved under accelerated approval represents benefit over available therapy or provide therapy where none exits.

In making a regulatory decision, you must be able to accurately assess a risk-benefit relationship. You must be able to have confidence in the benefit of the drug in relation to its toxicity. Your decision regarding the approval status of a drug should be based on the clinical risk-benefit decision, not simply a desire to provide drug access to patients. Access to a yet-to-be-approved drug can be accomplished thorough well-designed registration trials or expanded access programs.

Seeking drug approval exclusively with a single-arm trial is an inherently risky venture. Hence, we have strongly urged sponsors to consider these single-arm trials part of a comprehensive drug development plan that incorporates the early initiation of randomized trials to define clinical benefit.

Although single-arm trials are less expensive, less complex to conduct, involve fewer patients and are performed more rapidly than randomized trials, they frequently do not provide the information required by physicians and patients to make rationale therapeutic decisions.

If results are robust in a single-arm trial, then everyone wins—most importantly, patients receive needed therapies earlier. If results are nominal resulting in ambiguity regarding a risk benefit decision, randomized trials will be needed to accurately assess the drug. Unfortunately, this may delay drug approval.

In comparison to single-arm trials, randomized trials provide the opportunity to examine additional endpoints, such as survival, time to progression, and symptom benefit and more accurately characterize adverse events.

NCI Programs:

NCI Prostate SPOREs Plan Biospecimen Banking Project

By Kirsten Boyd Goldberg

NCI-funded Specialized Programs of Research Excellence in prostate cancer are planning a pilot project to develop a biospecimen bank, an Institute official said.

Anna Barker, NCI deputy director for advanced technologies and strategic partnerships, said the project would test the concept of the National Biospecimen Network proposed by C-Change and NCI last year.

"NCI must take a proactive role to provide the kind of highly annotated, high-quality biospecimens that investigators need," she said to the National Cancer Advisory Board at its meeting Nov. 30.

NCI provides $50 million a year to support biospecimen banking in 125 programs that maintain about 4 million biospecimens, a survey by Barker's office concluded recently.

The prostate SPOREs project is one of several activities the Institute is planning to improve biospecimen banking, Barker said. The NIH Foundation is planning to "pilot" the National Biospecimen Network, for all diseases, she said.

As a result of the survey, Barker's office developed the following recommended actions for NCI to take over the next year or several years:

--Create a biorepository/biospecimen oversight and review group within NCI.

--Convene a workshop to identify "best practices" and support the development of standard operating procedures.

--Develop a pilot program to implement best practices, potentially through the NCI-funded cancer centers and the Cancer Bioinformatics Grid (caBIG).

--Implement a common bioinformatics platform to track and account for biospecimens through caBIG.

--Develop a broadly accessible, comprehensive database inclusive of NCI-supported biospecimen resources.

--Support a research program in biospecimen banking research.

--Facilitate tracking of budget information for human biorepository-related activities through NCI's

financial database coding system.

The NCI Board of Scientific Advisors earlier this month established a Biospecimen Subcommittee to study the development of the proposed National Biospecimen Network.

"The concept of developing a national system which links available specimens with annotated clinical information and provides mechanisms for access by a wide range of investigators has widespread appeal," wrote BSA Chairman Robert Young, president of Fox Chase Cancer Center, in a proposal to the board to establish the subcommittee.

The group plans to work with NCI to develop a series of workshops in five areas: information technology needs; standard operating procedures; legal, HIPAA, and intellectual property issues; costs and mechanisms of support; access to specimens.

* * *

The Clinical Trials Working Group, a panel of NCI advisors and staff, has established a Web site to solicit recommendations about the cancer clinical trials system: http://ncicbforums.nci.nih.gov/ictQuestions/login_form.

"We are looking for insights from anyone interested in the future of cancer clinical trials," said NCI Division of Cancer Treatment and Diagnosis Director James Doroshow, chairman of the working group.

Users are required to enter the following password: CTWGstakeholder. The Web site will be open through Jan. 15.

* * *

EDRN update: NCI awarded $9.8 million in first-year funding for 17 Biomarkers Developmental Laboratories in the Early Detection Research Network.

The award marks the second round of five-year funding for components of the network. Of 68 applications received for the BDL awards, 22 were rated as excellent to outstanding, and 17 were selected for funding. About 40 percent of grantees are new to the network, which began in 1999.

The BDL will search hundreds of samples using a variety of technologies to identify candidate biomarkers to identify cancer and cancer risk.

The other components of the EDRN are Biomarker Validation Laboratories, which work to validate the biomarker tests; Clinical and Epidemiologic Centers, which conduct the early phases of clinical and epidemiological research on the application of biomarkers; and the Data Management and Coordinating Center, which provides logistical, informatics, and statistical development and support.

The BDL principal investigators, their institutions, and their industry collaborations, if any, are: **William Bigbee**, University of Pittsburgh Cancer Center, Biospect; **Timothy Block**, Drexel University, Xenomics Inc. and Immunotype Inc.; **Paul Cairns**, Fox Chase Cancer Center; **Arul Chinnaiyan**, University of Michigan, GMP Companies Inc.; **Bogdan Czerniak**, M.D. Anderson Cancer Center; **Laura Esserman**, University of California, San Francisco, Sequenom, Biotrue, BD Biosciences, Celera Diagnostics, Biospect, and ChromaVision; **Wilbur Franklin**, University of Colorado Health Science Center; **Adi Gazdar**, University of Texas Southwestern Medical Center, Rules-Based Medicine; **Samir Hanash**, Fred Hutchinson Cancer Research Center; Michael Hollingsworth, University of Nebraska Medical Center; **Anne Killary**, M.D. Anderson Cancer Center; **Alvin Liu**, University of Washington, MacroGenics Inc.; **Jeffery Marks**, Duke University Medical Center, Abbott Laboratories; **Stephen Meltzer**, University of Maryland School of Medicine; **Hemant Roy**, Evanston Northwestern Research Institute; **J. Oliver Semmes**, Eastern Virginia Medical School, Ciphergen; **David Sidransky**, Johns Hopkins University, Oncomethylome Sciences, Affymetrix.

Bush Signs Omnibus Bill

President George W. Bush signed the omnibus spending bill funding federal agencies on Dec. 8. The bill provides NIH with $28.37 billion, an increase of $571 million or 2.1 percent over FY 2004. The figure includes a government-wide, across-the-board reduction of 0.8 percent for all discretionary spending.

Before the reduction, NCI would receive $4.87 billion, an increase of $129 million, or 2.7 percent over last year. FDA would receive $1.46 billion, an increase of $76 million, which is $33 million below the amount Bush requested.

Funding Opportunities:

DoD Prostate Cancer Program

The Department of Defense Prostate Cancer Research Program has $85 million in FY 2005 to support research. The program has 12 different award mechanisms. Application due dates for six of the programs are Feb. 8 and four have a deadline of June 7. Details of the program announcements and deadlines, and electronic submission of forms are available at http://cdmrp.army.mil.

In Brief:

Univ. of South Alabama Wins $20M Federal Funds For Center

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Lisa K. Simmons Distinguished Chair in Comprehensive Oncology, professor of internal medicine, and associate dean for oncology programs at UT Southwestern.The medical center received a $15.4 million gift from the Harold C. Simmons Foundation to increase its cancer research program through faculty recruitment, which includes Willson's appointment. . . . **UNIVERSITY OF SOUTH ALABAMA** Cancer Research Institute will receive $20 million in federal funding for the current fiscal year, **Sen. Richard Shelby** (R-Ala.) said. The one-time appropriation is contained in the omnibus FY 2005 funding bill passed by Congress. . . . **CITY OF HOPE Cancer Center** was awarded a five-year, $11.5 million NCI Specialized Program of Research Excellence grant for translational research studies for Hodgkin's and non-Hodgkin's lymphoma, said **Michael Friedman**, president and CEO. The principal investigator is **Stephen Forman**, chairman, Division of Hematology and Hematopoietic Cell Transplantation. **Andrew Raubitschek**, director of Radioimmunotherapy, is co-principal investigator. . . . **MEMORIAL SLOAN-KETTERING** Cancer Center established the Louis V. Gerstner Jr. Graduate School of Biomedical Sciences, a doctoral program to train laboratory scientists to work in research areas directly applicable to human disease. "We need a specially trained cadre of young scientists to help make that quantum leap into 21st Century medicine," said **Harold Varmus**, MSKCC president. Gerstner was vice chairman of the MSKCC Boards of Overseers and Managers, chairman of the Board of Managers of Sloan-Kettering Institute, and currently serves as chairman of the Board of Trustees of the school. **Kenneth Marians**, program chairman of the Molecular Biology Program, was named dean of the graduate school. Beginning in July 2006, the school plans to enroll 10 to12 students in the program leading to a Ph.D. in cancer biology. By 2012, the program expects to enroll 60 students a year. . . . . **M. D. ANDERSON Cancer Center** completed construction of the Ambulatory Clinical Building and the Cancer Prevention Building. The new facilities will help meet the increasing demand for outpatient care and services, said **John Mendelsohn**, president of M.D. Anderson. The ACB will be the home of the Nellie B. Connally Breast Center, Laura Lee Blanton Gynecologic Oncology Center, the Genitourinary Oncology Center, a 75-bed ambulatory treatment center, and 590 patient exam rooms. The CPB will house the Division of Cancer Prevention and Population Sciences, which include the departments of Clinical Cancer Prevention, Behavioral Science, Epidemiology and Health Disparities, and the clinical activities of the Cancer Prevention Center. . . **UNIVERSITY OF NORTH CAROLINA** at Chapel Hill has received a 3-year, $1 million grant from the National Center for Research Resources for a Genome Fingerprint Scanning program. **Morgan Giddings**, assistant professor at the UNC School of Medicine, is the project director. . . . **ERIC HORWITZ** was appointed clinical director of the Department of Radiation Oncology at Fox Chase Cancer Center. A prostate cancer researcher and lead investigator of clinical trials involving radiation treatment techniques, Horwitz joined Fox Chase in 1997. . . . **JONATHAN SIMONS**, director of Winship Cancer Institute at Emory University, was presented the Medical Advancement Award from the Avon Foundation for his work to establish the Avon Foundation Comprehensive Breast Center at Grady Memorial Hospital in Atlanta. The foundation also recognized **Ann Curry**, news anchor for the NBC Today Show, and **Paul Boulanger**, president and founder of Boston-based Men with Heart. . . . **BRENDA CULLEN** was appointed manager of finance and administration by the Academy of Molecular Imaging. Cullen was with Hotchkis and Wiley, a former subsidiary of Merrill Lynch & Co. . . . **NIH** and the American office of the Rhodes Trust of the U.K. are funding doctoral research and education at Oxford University and at NIH for students who have been awarded a Rhodes Scholarship. The alliance encourages Rhodes Scholars with an academic interest in biomedical science to pursue leadership roles in medical research. The alliance will sponsor joint educational programs for the students about developments in the life sciences with broad reaching societal impact, said **Michael Lenardo,** director of the NIH/Oxford Program. . . . **AMERICAN SOCIETY OF CLINICAL ONCOLOGY** said it would fund a four-year $120,000 international educational and training fellowship program to improve the level of cancer care in developing countries. The International Cancer Technology Transfer Fellowship is awarded by the International Union Against Cancer. "We know from follow-up research that, on average, each fellow has learned and applied at least two new skills in their practice and they have passed that new knowledge on to roughly 20 of their colleagues," said **Alan Coates**, member of the ASCO International Affairs Committee. The ASCO funds also support the Reverse ICRETT fellowship, which sends experienced clinical oncologists to developing countries to hold training courses.

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Business & Regulatory Report

Clinical Trials:

Genomic Health Oncotype Assay Predicts Breast Cancer Recurrence, Response

The **National Surgical Adjuvant Breast and Bowel Project** and **Genomic Health Inc.** of Redwood City, Calif., announced findings that challenge the assumption that all women benefit similarly from chemotherapy.

A study presented at the 27th Annual San Antonio Breast Cancer Symposium and coincide with publication in the New England Journal of Medicine demonstrated that a Genomic Health panel of tests quantifies the

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Oncology Management:

NCCN Provides Drug and Biologics Compendium For Three Cancers

National Comprehensive Cancer Network of Jenkintown, Penn., released the first three chapters of the NCCN Drugs and Biologics Compendium covering appropriate use of drugs and biologics in the treatment of colon, rectal, and anal cancers.

"A variety of constituencies in the health care community look to NCCN for evaluative information to aid their decision-making," said William McGivney, CEO of the NCCN.

"NCCN again is responding to these needs by providing evaluative recommendations in an easy-to-use format," he said. "One target audience for the NCCN Drugs & Biologics Compendium comprises decision-makers at insurance and managed care companies who seek authoritative and definitive information to establish coverage policies. In cancer care, the issue of the appropriateness of use beyond FDA-approved labeling is critical and is addressed extensively by the compendium."

The compendium delineates the appropriate uses of drugs and biologics in the care of cancer patients, which are derived directly from the NCCN Clinical Practice Guidelines in Oncology.

The compendium will span the continuum of cancer care from early stage to advanced stage disease, from supportive care to palliative care, NCCN said. The document is available free of charge in electronic and paper formats.

Diseases are listed with indications and specific recommendations for use as described in the NCCN Guidelines, the network said. The document also defines the level of evidence and degree of consensus that support the recommendation. Future chapters of the compendium will concentrate

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

Genomic Health, NSABP Say Assay Predicts Response

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likelihood of breast cancer recurrence for a large portion of early stage breast cancer patients and predicts the magnitude of chemotherapy benefit in these patients.

The results demonstrate that the Oncotype DX panel quantifies the likelihood of recurrence in node-negative, estrogen receptor- positive breast cancer, the comoany and NSABP said.

"Our study discloses that the same 21-gene panel that we demonstrated could quantify breast cancer recurrence, can also predict response to chemotherapy," said Norman Wolmark, chairman of NSABP. "These data advance the state of the art in cancer care and call for a reevaluation of treatment practice. By using the Oncotype DX assay, physicians can more effectively optimize a treatment plan and avoid under treating and over treating breast cancer patients."

The NSABP B-20 chemotherapy benefit study of 651 patients demonstrated that breast cancer patients with high Recurrence Scores (and high risk of recurrence), as identified by the Oncotype DX assay, also have a large absolute benefit from chemotherapy.

This group represents about 25 percent of patients with node-negative, estrogen receptor-positive breast cancer. Patients with low Recurrence Scores (and low risk of recurrence) only derive minimal if any benefit from chemotherapy and represent about 50 percent of these patients.

"The development of this test reflects the cooperative efforts of breast cancer research groups, patient advocacy, industry, and the federal cancer research program," said JoAnne Zujewski, head of breast cancer therapeutics at the NCI Clinical Investigations Branch. "NCI's longstanding support of the clinical trial process and tumor tissue banks took years off the process needed to gather data to validate the test."

NSABP and Genomic Health also announced that the New England Journal of Medicine published the results of their large-scale, validation trial demonstrating that the Oncotype DX 21-gene assay quantifies the likelihood of breast cancer recurrence in a large portion of early stage patients.

The journal is publishing the study online as an early release to coincide with the NSABP data presentations at SABCS. The same study will appear in the December 30 print edition. The study showed that the "Recurrence Score" determined by Oncotype DX provides a level of correlation to breast cancer recurrence that exceeds standard measures, such as patient age, tumor size and tumor grade.

The results indicate that approximately half of patients are reclassified from low risk to higher risk, or from higher risk to low risk by the Recurrence Score. when compared to classification by existing guidelines based on the standard measures. These data, originally presented at the San Antonio symposium in 2003, represent the first large-scale, multi-center validation of a multi-gene assay.

"The Oncotype DX assay has been extensively evaluated in numerous independent studies involving over 2,600 breast cancer patients, including the large validation study now in the peer-reviewed New England Journal of Medicine," said Steven Shak, chief medical officer of Genomic Health. "We believe the Oncotype DX assay will become a standard of care in breast cancer, providing critical information to help physicians and patients make potentially life changing treatment decisions."

NSABP and Genomic Health performed a blinded validation trial with prospectively-defined endpoints using surgical tissue samples from 668 tamoxifen-treated patients, who had node-negative, estrogen receptor-positive breast cancer.

The tissue samples were from patients who enrolled in the NSABP B-14 clinical trial from 1982-1988 and whose outcomes have been tracked over time by NSABP sites. This was the first time that such a study had been conducted using thin sections

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from standard diagnostic pathology specimens (fixed paraffin-embedded tissue) that are routinely available, the company and the group said.

Using quantitative RNA analysis of tumor tissues, the study evaluated the ability of the 21-gene Oncotype DX Recurrence Score assay to determine the likelihood of breast cancer recurrence. The Recurrence Score was able to accurately assign individual patients into high and low risk groups ($p<0.001$), and when the Recurrence Score was examined together with age and tumor size in a multivariate analysis, the Recurrence Score was the strongest independent predictor of recurrence ($p<0.001$).

The NSABP validation study and the NSABP B-20 chemotherapy benefit study looked at a specific population of breast cancer patients, those with node-negative, estrogen receptor-positive tumors who were treated with tamoxifen. This represents about 50 percent of all newly diagnosed breast cancer patients in the US each year.

The NSABP validation study showed that using multiple genes is more powerful than using single genes and will provide more consistent and reliable information for physicians and patients. The 21-gene panel includes genes related to critical pathways that breast cancer cells depend on, including the estrogen receptor, HER2 and proliferation as well as several other important pathways.

* * *

Aventis, a unit of the Sanofi-Aventis Group, announced the formation of A Breast Cancer Registry of Adjuvant Strategies (ABREAST), an international prospective registry of patients with early stage breast cancer.

ABREAST will provide a current picture of real-life clinical practice as well as patient and disease characteristics, the company said.

This registry, using standard patient selection criteria, data collection instruments and definitions, will collect data on the treatment and outcome of 36,000 women and men, aged 18 or older, and will provide an understanding of existing and evolving practice patterns.

The ABREAST project will include randomly selected 1,000 centers in over 60 countries including academic medical centers, community-based facilities and physicians' offices.

Analyses of ABREAST data may reveal factors that influence treatment decisions, highlight clinical practice areas requiring education and provide supporting data and resources to include regional considerations in guidelines, the company said.

"ABREAST will provide physicians with detailed, real-world data from approximately 36,000 patients that may be more representative than information collected in controlled studies and provide insight into treatments and outcomes of patients with early stage breast cancer," said Joyce O'Shaughnessy, of Baylor Sammons Cancer Center, Texas Oncology, PA, one of five breast cancer experts on the ABREAST scientific committee.

"Data from ABREAST will be the first step in establishing a global database to assess current standards of care in early stage breast cancer such as surgery, chemotherapy, hormone therapy and radiation," O'Shaughnessy said. "It is our intent to disseminate this information to provide insight that will help physicians evaluate their treatment choices for their breast cancer patients in early stages."

ABREAST will enroll patients diagnosed with stage I or II breast cancer. Patients will be followed for five years. ABREAST will capture disease characteristics, including tumor size and nodal status, as well as biomarkers, such as hormone receptor status. The registry will collect information on whether patients are offered and whether they receive adjuvant or neoadjuvant treatments.

* * *

ImClone Systems Inc. (Nasdaq: IMCL) of New York said it has begun a phase I trial of its fully human monoclonal antibody targeting the epidermal growth factor receptor, IMC-11F8, for solid tumors.

The company said it received approval for the trial from the National Institute for Public Health and the Environment, the Dutch regulatory agency.

The two-center study of up to 40-patients will be conducted at the Free University in Amsterdam and Utrecht University, and is designed to evaluate the safety and pharmacology of the antibody administered weekly or bi-weekly by intravenous infusion, the company said.

IMC-11F8 binds to the EGFR, thereby inhibiting certain ligands, or growth factors, from binding to and activating the receptor, the company said. The action blocks a signal pathway to tumor growth and repair and has also been shown to induce or apoptosis, in human tumors in animal models.

"While we currently do not plan to develop this antibody in the U.S., we do intend to pursue an expedited development process in Europe," said Daniel Lynch, CEO of ImClone.

* * *

Flamel Technologies, S.A. (Nasdaq: FLML) of

Lyon said it has enrolled the first patient in a cross-over randomized phase I/II study of Flamel's Medusa formulation of long-acting interleukin-2 in comparison with Proleukin. Proleukin is the only treatment currently approved for renal cancer. The study is being done at the Necker Hospital in Paris, France. The lead investigators are Herve Fridman and Nicolas Thiounn.

Pre-clinical studies of Flamel's long-acting interleukin-2 versus Proleukin in monkeys showed an increase in the duration of action of the drug, with a lower blood concentration of drug after injection, the company said. Flamel's formulation resulted in measurable increases in levels of lymphocyte CD4 and CD8, and the soluble fraction of CD25.

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(Continued from page 1)

on acute myeloid leukemia, chronic myelogenous leukemia, lung cancer, kidney cancer, testicular cancer, non-Hodgkin's lymphoma, and breast cancer.

NCCN said a full compendium from the guidelines that address appropriate treatment for 97 percent of all cancer patients and all supportive care areas would be developed within 18 to 24 months. Information about NCCN Drugs & Biologics Compendium and other NCCN programs is available at (215) 690-0255 or www.nccn.org.

* * *

Genzyme Genetics, a business unit of Genzyme Corp., said it has added bone marrow engraftment (chimerism) analysis by polymerase chain reaction to its cancer diagnostic/prognostic testing services.

"The addition of the test to our hematology/oncology menu enables us to assist physicians in confirming successful bone marrow engraftments for leukemia patients," said Moacyr DaSilva, national medical director, Genzyme Genetics, based in Westborough, Mass.

Frequent monitoring of donor/recipient populations, using molecular techniques, is a component of transplant procedures. BME (chimerism) analysis by PCR provides a more sensitive assessment of successful engraftment than traditional non-molecular techniques, and is useful in monitoring nonablative allogeneic stem cell transplantations (mini-transplants), the company said.

Nonablative allogeneic stem cell transplantations result in the co-existence of donor and recipient cells within the patient known as mixed chimerism. The mini-transplant procedure targets recipients that might otherwise be considered poor transplant candidates and reduces costs by decreasing graft vs. host disease complications and hospitalization time, the company said.

The bone marrow engraftment test uses polymerase chain reaction technology to detect multiple, short-tandem repeats in donor and recipient samples, the company said. STRs are short, highly repetitive, polymorphic DNA sequences that vary in number of repeats from individual to individual. The use of PCR to detect and compare multiple STRs between donor and recipient provides sensitivity and specificity for accurate monitoring of chimerism in transplant patients.

* * *

I-Flow Corp. (Nasdaq: IFLO) of Madison Heights, Mich., said it has entered into a national agreement with **Aetna** to make available the I-Flow InfuSystem service for oncology therapy.

The system offers ambulatory infusion pumps and related disposable supplies from manufacturers while a team of health care providers manages the care assumes regulatory functions to achieve overall efficiency and cost-effective clinical outcomes, the company said.

InfuSystem enables oncologists to control the delivery of chemotherapy and directly manage progress of their patients without the need for a hospital setting or for them to receive treatment at home from a non-physician, the company said.

"Aetna provides benefits in 50 states ranging from small employers to those serving Fortune 1000 companies," said Steve Watkins, president of InfuSystem, a wholly-owned subsidiary of the I-Flow Corporation. "This greatly broadens the scope of patients who can benefit from the continuity of care and efficacy that this method provides, offering some measure of relief and comfort during cancer treatment."

* * *

The **Translational Genomics Research Institute** and the **International Genomics Consortium** of Phoenix have formed the **Molecular Profiling Institute Inc.**, a specialty reference laboratory that utilizes discoveries from the Human Genome Project to analyze cancers from individual patients.

"By identifying the individual molecular profile of a person's cancer, MPI helps oncologists and pathologists to provide better customized therapeutic options for their patients," said Robert Penny, CEO and president of MPI.

MPI completed its initial investment round by obtaining seed capitalization of $1.35 million.

MPI's first molecular profile program is called Target Now. Launched in September 2003, the program is now available to cancer patients for whom all standard therapies have failed. Patients can have their cancer sampled, profiled, and assessed to determine if one or more drug targets can be identified in their tumor tissue.

Utilizing proteomic and genomic technologies, MPI provides oncologists and pathologists with information they can use to determine therapeutic options for their patients—options that may not have been considered without information provided by the Target Now analysis, the company said.

"The launch of MPI is consistent with TGen's mission to do excellent science, find ways to move discoveries into the practice of medicine and to spawn the formation of for-profit companies," said Richard Love, Tgen's Chief Operating Officer. MPI was started in collaboration with Scottsdale Healthcare in laboratories at the Virginia G. Piper Cancer Center in Scottsdale.

The institute has also recently formed a strategic partnership with AmeriPath, an anatomic pathology laboratory company. Through this partnership, AmeriPath's pathologist network, which serves approximately 3.5 million patients, has access to the molecular profiling provided by MPI. AmeriPath will use MPI for its advanced reference lab and provide assistance with co-marketing and sales.

In another development, MPI entered into an initial licensing agreement with Netherlands-based Agendia where MPI is the sole source provider in the United States of MammaPrint, a microarray assay used to provide important prognostic information for individuals with early invasive breast cancer. The test will be available in January 2005 to breast cancer patients nationwide, the companies said.

Deals & Collaborations:

Adherex Completes Purchase Of Cadherin Biomedical

Adherex Technologies Inc. (AMEX: ADH) (TSX: AHX) of Research Triangle Park, N.C., said it has completed acquisition of **Cadherin Biomedical Inc.**

"This acquisition brings back to Adherex's portfolio the non-cancer applications of our Cadherin platform," said William Peters, chairman and CEO. "While Adherex will continue to focus on advancing our oncology drugs through clinical development, these non-cancer assets will likely be of interest to potential partners and the completion of this acquisition should strengthen our negotiating position. Further, it offers Adherex the opportunity to enter into licensing agreements to further the development of these assets and thereby provide another potential revenue stream to improve shareholder value."

Under the agreement, Adherex will issue to CBI shareholders 3.2 million shares of Adherex common stock in exchange for all of the issued and outstanding shares of CBI, or approximately 0.069 shares of Adherex common stock for each share of CBI preferred stock held (subject to any claims made against the 500,000 Adherex shares to be held in escrow), the company said.

The companies said the acquisition settles their past litigation.

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HealthTronics Inc. (Nasdaq: HTRN) of Austin, Tex., said it has entered into an agreement with **Qualigen Inc.**, of Carlsbad, Calif., to co-market its FastPack System and its PSA and Testosterone FastPack test kits.

The agreement allows HealthTronics to offer the services to the 3,000 urologists in its service network, the company said.

"With our Fastpack System, the urologist now can offer PSA and testosterone testing in the convenience of an office setting," said Paul Rosinack, president and CEO of Qualigen. "Also important --results can be given to the patient in minutes, rather than through the traditional method of referring tests to an outside laboratory where results may not be available for days."

The system is FDA cleared and tests conducted on the system are fully reimbursable through Medicare and other insurance carriers, the company said.

* * *

Iceland Genomics Corp. of Reykjavik said it has entered into an agreement with **Aclara BioSciences** (Nasdaq: ACLA) under which Aclara will utilize its proprietary eTag assays to analyze tumor samples provided by IGC to validate candidate biomarkers as indicators of disease progression.

Under the agreement, Iceland Genomics said it would provide to tumor and blood samples and blinded patient data, including treatment histories and outcomes. Aclara would test the samples with its eTag assays to validate the parameters measured as biomarkers. Aclara would also provide funding to IGC, and would share the data from the study with IGC for incorporation into its database.

The biomarkers under evaluation are proteins and protein complexes with different functional or activation

states that comprise signaling pathways in cells, the companies said.

The eTag assays are able to identify protein complexes that can provide information regarding which would patients respond to specific therapies, the companies said. Since eTag assays can utilize formalin-fixed paraffin-embedded clinical samples, the standard format in most pathology labs, the analysis of both archived samples from initial biopsies or surgeries as well as freshly collected materials is possible.

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Morphotek Inc. of Exton, Penn., said it has entered into a multi-product research collaboration and license agreement with **Novo Nordisk** (NYSE: NVO) for the Morphotek proprietary Morphodoma technology to develop high-affinity antibodies and high-titer antibody-producing mammalian cells for scaleable manufacturing.

Under the non-exclusive, multi-year agreement, Morphotek will receive an upfront payment and funding for research and development to optimize up to four independent products, the companies said. Morphotek will also receive a licensing fee and milestone payments upon the successful achievement of program goals and the advancement of the products through clinical development. Novo Nordisk will conduct the preclinical and clinical development and subsequent commercialization of all products.

The Morphodoma technology is a proprietary process that evolves antibody producer cell lines to yield monoclonal antibodies with increased specificity and binding affinity to target antigens and/or to create sublines with enhanced titer yields for scaleable manufacturing, the companies said.

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Nautilus Biotech of Paris and **Angel Biotechnology** of Northumberland, England, have signed an agreement for the manufacture of the Nautilus interferon alpha (Belerofon) for phase I development.

Nautilus said it has designed and developed an improved, single amino-acid substitution, non-pegylated interferon alpha (Belerofon) with superior biological and pharmacological profile compared to marketed pegylated interferon alpha. Belerofon is a product candidate for indications including chronic HepC and cancer. Its profile should support lower frequency of administration and lower dosing with higher therapeutic efficacy, the company said.

Belerofon, a variant of natural alpha interferon, has a longer half-life in serum compared to native alpha interferon, the company said. The produt has a superior pharmacological profile, with a half-life in primates equivalent to marketed pegylated alpha interferon products, which is expected to support the standard of care of once per week dosing schedule, used for PEG-IFN.

Product Approvals and Applications:

Pfizer Files sNDA For Aromasin For ER+ Early Breast Cancer

Pfizer Inc. (NYSE: PFE) of New York said it has submitted a supplemental new drug application for Aromasin (exemestane tablets) for the adjuvant treatment of postmenopausal women with estrogen receptor positive or receptor unknown early-stage breast cancer.

Results from the pivotal Intergroup Exemestane Study (IES), published in the New England Journal of Medicine, demonstrated that postmenopausal breast cancer patients who had been treated with two to three years of tamoxifen for early breast cancer and were switched to Aromasin significantly reduced their risk of recurrence and increased disease-free survival compared to patients who remained on tamoxifen for the entire five years.

Pfizer's announcement follows newly released American Society of Clinical Oncology recommendations on the use of aromatase inhibitors as adjuvant therapy for postmenopausal women with hormone-receptor-positive breast cancer and coincides with the presentation of an update on the study trial being used to support the filing.

The ASCO recommendations, published in the Journal of Clinical Oncology, included among its treatment options for women initially started on tamoxifen a switch to an aromatase inhibitor based on data from the Aromasin study, IES.

Charles Coombes, director of the Cancer Research UK Laboratories at Imperial College London, Hammersmith and Charing Cross Hospitals, presented an update from the IES at the 27th Annual San Antonio Breast Cancer Symposium, based on 37.4 months of median follow-up and 4,740 patients.

These findings showed that 193 women treated with exemestane experienced a local or distant recurrence of disease compared with 264 women who continued on tamoxifen. A 30 percent reduction in risk of recurrence in breast cancer was reported when women were switched to Aromasin after two to three years of tamoxifen, compared to those who continued on tamoxifen for a total of 5 years, the current standard

of care (P=0.00005).

In addition 54 percent fewer cases of contralateral breast cancer (12 vs. 26) developed in women treated with Aromasin compared to those who remained on tamoxifen (P=0.04).

Aromasin was approved in the US in 1999 for the treatment of advanced breast cancer in postmenopausal women whose tumors have stopped responding to tamoxifen. It also is approved for use in Europe, Japan, and South America.

Unlike other aromatase inhibitors, exemestane is a steroidal aromatase inactivator, which means it selectively targets and irreversibly binds to the aromatase enzyme, which is required to produce estrogen, the company said.

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Active Biotech of Lund, Sweden, said FDA has granted Fast Track status to TTS CD3 for non-small cell lung cancer.

A phase I study with TTS CD3 is underway, and the phase II/III program is planned for 2005, the company said.

In parallel with the ongoing phase I studies, Active Biotech said it intends to start a clinical study to examine the safety of TTS CD3 in combination with established chemotherapies of non- small cell lung cancer.

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Amgen Inc. (Nasdaq: AMGN) of Thousand Oaks, Calif., said FDA has granted Fast Track designation for two experimental therapies, AMG 531 and AMG 706.

AMG 531 received orphan drug designation in 2003, the company said.

"AMG 531 is our first peptibody and represents a new approach to treat immune thrombocytopenic purpura, an autoimmune bleeding disorder," said Beth Seidenberg, chief medical officer and senior vice president of global development at Amgen. "AMG 706, our first investigational oral cancer therapy, may hold promise for various tumor types and is in phase II trials for imatinib-resistant gastrointestinal stromal tumors."

As an investigational platelet growth factor, AMG 531 stimulates platelet production and could shift the treatment focus from preventing platelet destruction to boosting platelet production in patients with ITP, the company said. The therapy is an engineered protein therapeutic, a peptibody, that provides targeted action--in this case, on the thrombopoietin receptor. Like TPO, AMG 531 binds to the TPO receptor and stimulates precursor cells of platelets, called megakaryocytes, to mature into platelets.

In phase I and II studies, AMG 531 enhanced platelet production in patients diagnosed with ITP, the company said. AMG 531 has been generally well tolerated. The most frequently reported adverse events were bruising, nosebleeds, headache and mouth blisters.

AMG 706 is an oral multi-kinase inhibitor that targets vascular endothelial growth factors, platelet derived growth factor, Kit and Ret receptors, the company said. Through the combined action of Kit and PDGF receptor inhibition, coupled with VEGF receptor inhibition, AMG 706 provids more than one mechanism of action in cancers. Activating mutations of Kit or PDGF receptors are critical to the pathogenesis of more than 90 percent of GIST.

Early clinical data show signs of tumor regression with promising preliminary safety data that may allow for combination therapy, the company said. AMG 706 is being evaluated as both a monotherapy and in combination with other agents for cancers, including imatinib-resistant GIST, non-small cell lung cancer and colorectal cancer.

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Eastman Kodak Co. of Rochester, N.Y., said it has received FDA approval for its mammography computer-aided detection system.

"The availability of an innovative CAD system brings another new dimension to Kodak's portfolio of advanced mammography products," said Wido Menhardt, general manager of the CAD business, health imaging group at Kodak. "Kodak's fast and highly reliable analog mammography CAD system is our first CAD product for breast cancer detection."

The mammography CAD software integrates into existing radiology workflow, the company said. The user interface is intuitive and the system is small enough to fit in most healthcare facilities.

The software uses algorithms to identify areas on digitized mammograms for close examine during a second review, the company said. Clinical trial data document 39.4 percent of missed breast cancers could have been detected 14.8 months earlier using the technology.

Kodak Health Imaging Group is also expanding from a business focused on radiology and dentistry into a healthcare information solutions provider serving more customers across healthcare organizations and within medical specialties, the company said. The expansion plans include combining the information technology with the Kodak digital-imaging science to offer hospital departments advanced clinical information systems, while marketing existing and new products across

medical specialties.

The product portfolio of the group includes computed radiography and digital radiography systems, laser imagers, picture archiving and communications systems, radiology information systems, traditional mammography systems, x-ray film systems for general radiography, and dental imaging products, the company said. Its services portfolio includes basic repair and maintenance, to professional services encompassing equipment integration (from multiple vendors), storage and archiving, secure email--and more.

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EDDA Technology of Princeton Junction, N.J., said it has received FDA clearance to market IQQA-Chest software, an image analysis system for the softcopy review of digital chest radiographic images.

The software carries the CE mark, and was also cleared by the Chinese State Food and Drug Administration for marketing and production in October 2004, the company said.

IQQA-Chest offers tools for identification and for the quantification of nodules detected with projection chest radiography, the company said. In identifying nodules, physicians are able to use lesion-specific image enhancement viewing modes that detail image structures and highlight areas suggesting nodular abnormalities. Once nodules are identified, the software offers regional analysis tools for the quantification of lesion characteristics including size, density and shape.

Combining lesion-specific image enhancement viewing and region of interest evaluation tools, the software is designed to identify, confirm and quantify of pulmonary lesions, the company said.

The software offers DICOM connectivity and automatically assembles diagnostic information into a clinical report for follow-up review. The plug-and-play software runs on standard PC platform.

"Bridging the detection of pulmonary nodules with accurate characterization, IQQA-Chest bolsters the image quality and workflow efficiency advantages of thoracic digital X-Ray," said Jian-Zhong Qian, president and CEO of EDDA Technology. "This combination will have a broad impact on improving nodule case diagnosis and patient prognosis, especially as digital X-Ray continues to gain market acceptance and acceleration."

Trial data demonstrated the software reduces inter-observer variation and improves the detection rate of actionable nodules, especially small nodules (5-15mm) that are more likely to be overlooked, the company said. The trial was conducted by Wei Song and Zhenyu Jin at the Peking Union Medical College Hospital in Beijing. The study reviewed 232 chest DR cases by physicians of different experience levels.

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U.S. BioDefense Inc. (OTCBB: UBDF) of City of Industry, Calif., said it has entered into a commercial evaluation agreement with NIH for universal vaccination of viruses, parasites, and tumor cells also developed with support by NCI.

The inactivated agents, which can be used as vaccines against the diseases caused by viruses, parasites and tumor cells, can be safely used for vaccination without the threat of infection because the immunogenic of the agent as a whole is maintained, the company said.

U.S. BioDefense said it intends to conduct laboratory, to evaluate the suitability for commercial development, and to provide the facilities, personnel, and expertise to evaluate the commercial applications.

Vaccination against pathogens has been one of the major accomplishments of medicine over the past century. While effective vaccines have been developed for a large number of diseases, development if a safe and effective vaccines for a number of other diseases remain problematic.

The use of inactivated or killed microbial agents as a vaccine, although generally safe, will not always be effective if the immunogenic characteristics of the agents are altered, the company said. The preferential degradation of certain antigens on the inactivated microorganism might produce a weak or poorly targeted immune response that permits a pathological response when the host is later challenged with the live microorganism.

It is therefore desirable to improve methods for inactivating agents such as virus, bacteria, cancer cells and other cell types, where the methods are capable of inactivating the agents without causing substantial degradation of the antigenic structure of the agents, the company said.

The inactivated agents should be useful as vaccines and free from adverse side effects at the time of administration as well as upon subsequent challenge with the live agent.

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Correction: An item in the November issue of Business & Regulatory Report should have read: **The Lance Armstrong Foundation** of Austin, Tex., gave a five-year, $500,000 to the **Nevada Cancer Institute** to establish the **Lance Armstrong Foundation Survivorship Center**.