THE CANCER LETTER

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Payline For NCI R01s Falls To 16 Percent, Where It's Likely To Stay In FY 2006

By Kirsten Boyd Goldberg

The NCI payline for investigator-initiated R01 grants will drop from the 20th percentile to the 16th percentile this fiscal year, and it's likely to stay at that level next year, Institute Director Andrew von Eschenbach said.

"Last year, we planted a flag in the sand and said we would maintain the R01 payline at 20 percent and we would adjust everything else around that," von Eschenbach said to the NCI Board of Scientific Advisors and Board of Scientific Counselors.

"In 2004 we met that commitment," he said. "In 2005, we will not be

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In Brief:

Mass. Residents Support Bill To Encourage Human Stem Cell Research, Survey Finds

SUPPORT FOR STEM CELL RESEARCH: 81 percent of Massachusetts adults support a state bill that would encourage stem cell research, permit somatic cell nuclear transfer, which is used to create stem cells for medical research, and ban cloning to create new human life, according to a survey conducted for Results For America, a project of the nonprofit Civil Society Institute, of Newton, Mass. Support for the pending state bill is strong across the board, including Catholics (76 percent), Republicans (66 percent), and small town/rural residents (81 percent). "This survey shows widespread public support for swift legislative action to encourage more stem cell research in Massachusetts so that our world-class researchers and other scientists can keep the lead in the global search for possible cures to Parkinson's, Alzheimer's, and other diseases," said **Gail Pressberg**, senior fellow at CSI. "These findings make it clear that the few vocal opponents out there are really speaking for almost no one other than themselves." . . . **UNIVERSITY OF CALIFORNIA, LOS ANGELES**, formed the Institute for Stem Cell Biology and Medicine to conduct embryonic and adult stem cell research that may lead to better treatments for HIV, cancer, and neurological disorders. UCLA will provide $20 million over five years to enable teams of researchers to compete for state grants created by the passage of Proposition 71. The money will pay for recruitment for a dozen new faculty positions, salaries, and expansion of laboratory space, infrastructure, and supplies. "As one of the world's leading research universities, UCLA has long been engaged in adult and embryonic stem cell research with activities in areas ranging from the AIDS Institute to the Brain Research Institute to

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Flat Budget Will Cause Pain, NCI Will "Exercise Courage"

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able to maintain the R01s at 20 percent. It's going to fall to 16 percent."

Scientists view the R01 payline, the ranking by peer review that serves as a cutoff for funding, as an important measurement of the research budget's ability to support scientific opportunities. During the early 1990s, frustration with paylines in the mid-teens caused scientists and patient advocates to lobby Congress to double the NIH budget.

"We have to begin to prepare the community that there will be flattening with regard to what they will be receiving," von Eschenbach said at the March 7 meeting. "Every time we say yes to something, by definition, it's no to something else. There is not one single decision that we will make this year that will not involve pain for someone."

For FY 2006, the Bush Administration proposed a 0.3 percent, $16 million increase for NCI, bringing the Institute's budget to $4.824 billion. NCI must give most of the new funds to NIH for various initiatives, von Eschenbach said.

The overall success rate for research project grants would be around 20 to 21 percent under the budget proposal, he said.

The President's budget doesn't include inflationary increases for non-competing grants, and the average cost of competing grants will remain the same in FY06 as in FY05.

However, the NCI director maintained that the Institute anticipated "all of those issues" two years ago and began planning to "redeploy" its resources.

"We will not simply remain in a steady state, but we will strategically grow the programs and initiatives that are essential to continuing to move the pace of progress forward, across the discovery, development, delivery continuum, in order to meet our goal of eliminating the outcome of cancer—suffering and death due to the disease," von Eschenbach said to the advisory boards.

The situation will require NCI officials and their extramural advisors to make difficult budget decisions, von Eschenbach said.

"One of the most significant qualities that a cancer patient possesses is the quality of courage," von Eschenbach said. "Just as that cancer patient has that quality of courage to face uncertainty, the leadership of NCI will, in fact, exercise courage in the face of uncertainty to make those decisions…. [T]here are great opportunities that must be achieved and embraced, and … we are going to have to do that in the context of not having unlimited resources."

BSC member Richard Kolodner, professor of medicine at the University of California, San Diego, said NCI also will need one more thing. "While I appreciate the seriousness of your tone, I think what's called for, more than courage, is wisdom," he said.

"I would be remiss in not stating that I worry about that a lot, because modest budget problems, combined with redirection of funds, have absolutely enormous potential for disrupting very valuable enterprises that you will not want to be without, and will miss when they are gone," said Kolodner, head of the Ludwig Institute for Cancer Research at UCSD. "So, I would just like to echo that you are in the midst of a rather serious situation where a lot of thought and wisdom is required, maybe more so than courage."

VON ESCHENBACH: "It can really turn into a 'Wizard of Oz' story. You need three things."

KOLODNER: "I'm hoping you're a wizard."

NCI's "Opportunity To Provide Leadership"

"These are the best of times, and, they are not the worst of times, but they are, certainly, the most challenging of times," said von Eschenbach.

"The reality is, at a budget of $4.8 billion, we have never had as much in the way of resources," von Eschenbach continued. "[NCI] still remains the single largest institute at the NIH. We have never had as many

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investigators, and never had as much intellectual capital invested in cancer research, and we still fund more cancer grants than any other grants in the entire NIH. So we are still in a very significant, very powerful position of leadership.

"That is the incredibly important theme that we have to exercise over these upcoming months and over these next few years: that it is the NCI's opportunity to not simply provide support for the cancer research enterprise, but to provide leadership for it.

"And that leadership is also, on the part of all of us, going to require courage, because it's going to require making decisions, and, in fact, making choices, in the face of uncertainty.

"There is much that we are obligated to do, there is much that we are being asked to do, but there is, importantly, much that we need to do. We need to move this agenda forward.

"We will find ways to partner, we will find ways to leverage, we will find ways to streamline and eliminate waste wherever we find it by finding more effective strategies for management, for integration of programs."

The NCI budget "is the largest commitment to cancer research in the world, but it is not the only commitment," he said.

Just as cancer centers leverage their NCI funding to seek philanthropic support, "we will be looking for investments as we go forward that are not only leveraged, but are investments which also provide leverage," he said.

Exceptions Funding Released

Von Eschenbach said he had released funding to allow NCI division directors to provide money for grant "exceptions" to the payline.

"We will make certain to continue to place a high priority on young investigators and first-time R01s," he said. "With the payline dropping, we may need to make more exceptions for first-time R01s. We will protect the young investigators."

Also, he sought to assure the extramural advisors that NCI "will continue to aggressively manage the intramural program," which would receive $717.9 million in FY06.

"The problem we are faced with is, there is nothing bad in the portfolio," von Eschenbach said. "There really isn't an area which you could look at and say, 'This is really of very little value.' Everything we have in this portfolio is very good. It isn't a matter of choosing something that's bad versus something that's good. It's a matter of choosing among goods.

"We will be putting in place this year specific mechanisms that will allow us to really drill down into the portfolio in a much smaller grain size than we ever had the need to do before, so that we are able to make much finer, discriminating decisions about the decisions we are making," he continued.

"We are also taking account that we are anticipating beyond 2006 that this trajectory of a flat budget is likely to continue. If not, it certainly will never, immediately in the next few years, go back to the era we had five years ago of double-digit increases."

Ethics Rules Cause "Stress And Anxiety"

The new NIH conflict of interest rules that went into effect Feb. 3 have affected morale and "created a great deal of stress and confusion and anxiety," among NCI staff, von Eschenbach said to the advisory boards.

The NCI director said he has encouraged staff members to submit comments on the rules to NIH. "As we can express where the rules are having unintended consequences that are negative in their impact, to bring that clarity to the process, in an appropriate way, gives us an opportunity to change the process," he said.

The public comment period is open until April 4. The rules are posted at www.nih.gov/about/ethics_COI.htm.

National Academies:

NIH Can Foster Independence, Originality In New Investigators

NIH can foster independence among new investigators by improving their raining and providing them more resources to pursue independent projects, according to a report by the National Academies' National Research Council.

NIH should provide postdocs and early-career investigators with more financial support for their own studies, and limit the maximum length of time they can spend in training under senior NIH-funded scientists to a total of five years, the report said.

Concerns have been raised for decades about scientists spending longer periods of time as postdoctoral appointees, unable to set their own research directions. In 2002, the median age at which researchers with Ph.D.s received their first independent grant from NIH was 42. In 2003, investigators under the age of 40 received less than 17 percent of the agency's competitive research awards—down from more than 50 percent in 1980. New

NIH policies and practices are needed to reverse the trend of ever-longer training periods, the report says.

"Science would benefit from a system that actively encourages new investigators to try out novel ideas and approaches," said committee chairman Thomas Cech, president of the Howard Hughes Medical Institute, and distinguished professor of chemistry and biochemistry, University of Colorado, Boulder. "Now is the time for action. Our report offers a plan to help ensure the continued vitality of the biomedical research enterprise and its work force."

Postdoctoral training provides aspiring researchers with critical skills and experiences that aid their transition to jobs as independent investigators, but this training period should be temporary, the report emphasizes. NIH and many academic institutions and scientific organizations have agreed in principle to a five-year limit on postdoctoral appointments. However, few mechanisms are in place to enforce this limit. To tackle the issue, NIH and other institutions should implement and enforce a policy that prohibits individuals from working as postdoctoral researchers for more than five years total—regardless of the type of award or grant they work under. If postdocs continue to work in the same laboratory after reaching the five-year limit, the continuation should be treated as a change in career track—accompanied by promotion to a "staff scientist" position with employee benefits and appropriate levels of responsibility, the report says.

In most cases, biomedical postdocs are paid through R01 research grants that are made to principal investigators. Consequently, postdocs are often required to spend their time focused on the research of these senior investigators, a pattern that may stifle their creativity. The report says NIH should move some of the resources for postdoctoral support from R01 grants to training grants and individual awards that aid postdoctoral work, such as the Ruth L. Kirschstein National Research Service Awards. Doing so would increase the number of awards made to individual postdocs, enhance oversight of training, facilitate collaborative research, and encourage young researchers to play bigger roles in the design and direction of their work.

To complement existing NRSAs, NIH should create a new independent-research award that enables postdocs to identify, explore, and control their own projects under the mentorship of senior investigators. The new awards should be portable—allowing selected postdocs to use them anywhere—and large enough to cover their salaries and job benefits.

Scientists from outside the U.S. play a critical role in the nation's biomedical research enterprise, the report notes. Either U.S. citizenship requirements for NRSAs and related postdoctoral training grants should be dropped, permitting researchers who are not U.S. citizens or permanent residents to compete for the funds, or equivalent avenues of support should be made available to these scholars.

Scientific research is enhanced by effective training and mentoring, the report adds. NIH should revise the R01 grant application and review process so that PIs seeking funds for postdoctoral research positions would have to describe not only how postdocs would contribute to proposed projects, but also how they would be prepared for independent careers. Furthermore, applicants for R01 grants seeking postdoc assistance should be required to provide lists of current postdocs as well as the names, laboratory tenure, and present job status of all postdocs supported in the past decade—information similar to that requested on training grant applications. Universities, academic departments, and research institutions should provide postdocs with more opportunities to learn professional skills such as grant writing and laboratory management.

To better track and analyze the effectiveness of relevant grant programs and funding practices, NIH should improve data collection on the progress of all postdocs. And it should evaluate different models of supporting their work, including the proposed new award for independent research, the committee said.

The agency now offers a collection of K22 career-transition awards to facilitate the move from postdoc to independent researcher. This program's confusing array of requirements limits its ability to foster independence more broadly, the report says. NIH should replace K22 awards with a new agencywide grant program that backs innovative research by scientists who are moving into their first jobs as independent investigators.

Each year the proposed career-development grant program should provide 200 grants worth $500,000 apiece, payable over five years. These new awards should offer postdocs up to two years of financial support to develop independent research projects, under the guidance of a mentor. After obtaining a fully independent research position, awardees could use the remaining funds for the next three to four years to grow their projects and develop professionally, the report says. The award would have uniform requirements and conditions across all NIH institutes, and it would not be limited to in-house candidates or previous fellowship recipients.

The report also recommends the removal of a major

barrier to new investigators' access to research funds. Currently, R01 grant applications require candidates to submit preliminary data predicting the success of proposed projects. But early-career researchers who want to conduct research unrelated to their postdoctoral work for senior investigators often have not had the time or resources to obtain such data. NIH should create a "New Investigator R01" award that would require a discussion of previous experience instead of preliminary data. The awards should have the same requirements across the agency, as well as budgets similar to other R01 grants. Also, they should have a five-year term, giving researchers time to establish laboratories, train personnel, and collect data without having to worry about immediately finding more research dollars.

The number of staff scientist positions that are not on the tenure track continues to grow, the report notes. NIH should start a grant program to support small science projects by these "soft-money" investigators, whose job security typically depends on external funding. Moreover, the agency should reserve funds to provide competitive, merit-based awards for the most talented staff scientists who run out of other research support. This money would serve as a bridge or safety net while they apply for other grants. The institutions where such scientists work should offer them multiyear, renewable contracts that guarantee office space, a salary, and minimal research assistance—even in the absence of external funding.

The study was sponsored by NIH.

Copies of the report, "Bridges To Independence: Fostering The Independence Of New Investigators In Biomedical Research," will be available at www.nap.edu.

FDA News:

FDA Issues Final Guidance On Pharmacogenomics

FDA earlier this week issued a final guidance to industry on "Pharmacogenomic Data Submissions."

Pharmacogenomics may allow health care providers to identify sources of an individual's profile of drug response and predict the best possible treatment option for the individual. This technology has enabled the development of targeted therapies including Herceptin for metastatic breast cancer, Gleevec for chronic myeloid leukemia and Erbitux for metastatic colorectal cancer.

"FDA's efforts will bring us one step closer to 'personalizing' medical treatment," said Janet Woodcock, FDA acting deputy commissioner for operations. "This new technology will allow medicines to be uniquely crafted to maximize their therapeutic benefits and minimize their potential risks for each patient."

FDA also recently approved the first laboratory test, the Amplichip Cytochrome P450 Genotyping Test, which will enable physicians to use genetic information to select the right doses of certain medications for cardiac, psychiatric diseases and cancer.

The guidance documet clarifies how pharmacogenomic data will be evaluated. The final guidance describes what data will be needed during the marketing application review process, the format for submissions, and the data that will be used during regulatory decision making. The guidance also explains a new mechanism for industry to voluntarily submit research data to further the scientific exchange of information as we move into more advanced areas of pharmacogenomic research. The voluntary data, which will be reviewed by an internal, agency-wide group and will not be used for regulatory decision making, will help FDA and industry gain valuable experience as this new field continues to evolve.

FDA's new pharmacogenomics Web page is available at http://www.fda.gov/cder/genomics/default.htm. The site includes detailed information on submitting genomic data, including a decision tree to simplify data submissions, relevant regulatory information, and FDA contact information.

FDA and the Drug Information Association have scheduled a meeting, "Pharmacogenomics in Drug Development and Regulatory Decision Making," from April 11-13, at the Mariott Hotel in Bethesda, Md.

The meeting will focus on integrating pharmacogenomics in clinical trials for new drugs, biologics, and associated devices. FDA will also address ways to translate pharmacogenomics into medical product development and clinical practice.

Professional Societies:

Blackburn, Rowley Win Landon-AACR Prizes

Two scientists whose fundamental discoveries into the cause and progression of cancer opened new paths for treatment will receive prizes for their work at the American Association for Cancer Research annual meeting next month.

Elizabeth Blackburn, the Morris Herzstein Professor of Biology and Physiology at University of California, San Francisco, will receive the Kirk A.

Landon-AACR Prize for Basic Cancer Research.

Janet Rowley, the Blum-Riese Distinguished Service Professor of Medicine and Molecular Genetics & Cell Biology at University of Chicago Medical Center, will receive the Dorothy P. Landon-AACR Prize for Translational Cancer Research.

The prizes, offered by the Kirk A. and Dorothy P. Landon Foundation and AACR, are the largest awarded to cancer researchers by a professional society of their peers. Each recipient will receive $200,000 and present a lecture at the AACR meeting, scheduled for April 16-20 in Anaheim, Calif.

Blackburn has investigated the structure and role of telomeres, the tips of genetic material at the end of chromosomes. She showed that telomeres consisted of a series of tandem repeats of a simple DNA sequence. This work set the stage for a second discovery, published in 1985 with then-graduate student Carol Greider, of telomerase, an enzyme needed if telomeres are to replicate. Though telomerase was found to be critical for normal cell growth, it also was found to play a role in the uncontrolled growth of cancer cells. Scientists now recognize that 80 to 90 percent of all cancer cells contain lengthened telomeres, with relatively large quantities of telomerase.

More recently, Blackburn has been working on the development of an anti-cancer therapy that forces cells with active telomerase to make errors during telomere synthesis, effectively triggering cellular suicide.

Rowley is being honored for her contributions to the understanding of how chromosomes can exchange genetic material, resulting in the uncontrolled growth of cells that characterizes cancer. She discovered the first such "translocation" in early 1972, while sorting through photographs of chromosomes from a patient with acute myelogenous leukemia. In this case, she observed that chromosome 8 appeared to trade genetic material with chromosome 21; part of 21 had broken off and moved to chromosome 8, and part of 8 had moved to 21.

Later that same year, she discovered that another defect linked to chronic myelogenous leukemia, known as the Philadelphia chromosome, also resulted from a translocation between chromosomes 9 and 22.

Rowley and colleagues have since identified several additional chromosomal translocations characteristic of other malignancies, such as the 14;18 translocation seen in follicular lymphoma; and the 15;17 translocation that causes acute promyelocytic leukemia.

This work set in motion the current era of cancer genetics, which has served as a foundation for the identification and validation of new drug targets.

Society Calls For Regulation Of Dietary Supplements

In a position paper released at its annual meeting earlier this month, the American Society for Clinical Pharmacology and Therapeutics called for improved labeling and stronger FDA oversight of dietary supplements.

"Consumers believe that dietary supplements are subject to regulations similar to over-the-counter drugs and that they've been reviewed by the FDA," said Jason Morrow, of Vanderbilt University and chairman of the ASCPT task force that produced the position paper. "Many supplements contain active ingredients that have the potential for serious, adverse effects—even at standard doses. Very little research has been done concerning dietary supplement safety."

The ASCPT paper urges Congress to make changes in the 1994 Dietary Supplement Health and Education Act to ensure dietary supplement safety. The society called for improved labeling of these products, reporting of adverse events associated with supplement use, educational materials for both health care professionals and consumers, and adequate funding that will enable FDA to conduct effective oversight and necessary research to assure dietary supplement safety.

The report also calls for FDA to work more closely with NIH in setting a rigorous research agenda for dietary supplements and to explore issues such as safety and efficacy by working with the USP (U.S. Pharmacopeia) in the verification of dietary supplements.

"Many studies have found great inconsistencies in the amounts of active ingredients in supplements, despite manufacturers' claims," Morrow said.

The position paper appears in the March issue of Clinical Pharmacology and Therapeutics.

Funding Opportunities:

DoD To Provide $4.25 Million For CML Research In FY05

The fiscal 2005 Defense Appropriations Act provides $4.25 million to the Department of Defense Chronic Myelogenous Leukemia Research Program (CMLRP). This program is administered by the U.S. Army Medical Research and Materiel Command through the Office of Congressionally Directed Medical Research Programs (CDMRP).

1) Exploration--Hypothesis Development: These awards are intended to support initial exploration of innovative, untested, potentially groundbreaking concepts in CML. Preliminary data is not required, although sound reasoning and a feasibility assessment are integral

components. Investigators at all levels are encouraged to apply. The maximum funding amount is $150,000, inclusive of direct and indirect costs, for a performance period of up to 24 months. Approximately ten awards will be made. The deadline for submitting electronic proposals is June 7, 2005 at 5 p.m. Eastern time.

2) Therapeutic Development Award: These awards are intended to sponsor preclinical assessment of therapeutics for CML. No total dollar amount restrictions; however priority will be given to smaller-scale, cost-efficient projects. Eligible investigators are Independent CML investigators. The deadline for submitting electronic proposals is June 7, 2005 at 5 p.m. Eastern time.

A detailed description of this mechanism, including evaluation criteria, specific submission requirements, and deadlines will be available in the FY05 CMLRP Program Announcements. Program Announcements are available at http://cdmrp.army.mil.

NIH Director's Pioneer Award

NIH is accepting nominations for the 2005 NIH Director's Pioneer Award through April 1.

This program, a High-Risk Research Initiative of Research Teams of the Future, is meant to complement NIH's traditional, investigator-initiated grant programs by supporting individual scientists of exceptional creativity who propose pioneering approaches to major contemporary challenges in biomedical research. Self-nominations should be submitted online at http://nihroadmap.nih.gov/pioneer/NominateSelf.aspx.

Program Announcement

Stem Cells and Cancer

The objective of this Program Announcement is to encourage research in the area of tumor stem cells, including research on the generality of the occurrence of tumor stem cells in solid tumors and hematologic malignancies. Research in all areas of tumor stem cell molecular and cellular biology will be encouraged. In addition, we will encourage investigators performing research in the areas of normal adult stem cells and embryonic stem cells to apply their expertise to investigating tumor stem cell biology.

Inquiries: R. Allan Mufson, Cancer Immunology and Hematology Branch, NCI Division of Cancer Biology, phone 301-496-7815, email: mblehar@mail.nih.gov.

RFA Available

Minority-Based Community Clinical Oncology Program

This RFA seeks to strengthen the Minority-Based Community Clinical Oncology Program by: 1) continuing the program as a vehicle for supporting participation of minority individuals in cancer treatment and prevention and control clinical trials through research bases (i.e., clinical cooperative groups and cancer centers supported by NCI); 2) expanding and strengthening the cancer prevention and control research effort; 3) utilizing the Minority-Based CCOP network for conducting NCI-assisted cancer prevention and control research; and 4) evaluating on a continuing basis Minority-Based CCOP performance and its impact in the community.

Participating community programs (Minority-Based CCOPs) will be required to enter participants onto NCI-approved cancer treatment and prevention and control clinical trials through the research base(s) with which each Minority-Based CCOP is affiliated. Minority-Based CCOPs may contact NCI program staff directly for assistance and participation in selected cancer prevention and control protocols. Minority-based CCOP performance will be evaluated on a continuing basis by the NCI program director.

Minority-Based CCOP applicants must demonstrate the potential for accessing appropriate cancer patients/participants within their communities for participation in cancer treatment and prevention and control protocols provided by their research bases.

Inquiries: Worta McCaskill-Stevens, Community Oncology and Prevention Trials Research Group, NCI Division of Cancer Prevention, phone 301-496-8541, email: mccaskiw@mail.nih.gov.

NCI Supplements Available

NOT-CA-05-016: Notice of Availability of Administrative Supplements for Disseminating Evidence-Based Intervention Research Products

Application receipt date: May 30

NCI is requesting applications for administrative supplements for NCI-funded cancer control intervention research R01, P01, P50, U01, and U19 grants. Applicants may apply for a supplement to a related R01, P01, P50, U01, or U19 intervention research award, as long as the following conditions are met:

1) The focus of the awarded grant is similar to the focus of the intervention dissemination supplement that is being proposed;

2) There are no funds in the related award related to the proposed dissemination effort;

3) There must be an active parent grant during the entire funding period of this supplement; and

4) The Principal Investigator for the supplement must be the Principal Investigator of the parent grant.

These supplements have been designed to provide 1-year funding to cancer control investigators whose intervention efficacy data have been analyzed and who are conducting peer-reviewed research (with an active NCI grant award) related to the intervention program proposed for dissemination. Intervention research across the cancer control continuum that may be eligible for these supplements, includes: tobacco use prevention and cessation; promotion of appropriate changes in diet and physical activity; reduction of sun exposure and ultraviolet (UV) radiation exposure; facilitation of informed decisions about genetic testing

for cancer susceptibility; enhancement of screening for breast, cervix, and colorectal cancers; quality of care; and improvements in coping skills and quality-of-life for cancer survivors and their families. Detailed instructions for applying for this supplement are posted at www.dccps.cancer.gov/funding_apply.html#dd.

The application should take the form of a request letter that contains sufficient detail (similar to a standard research application) to allow assessment of the scientific merit of the proposed dissemination plans and the appropriateness of the request for supplemental funding (see web site for more detailed application information). Budgets should not exceed $125,000 in direct costs for a time period not exceeding 12 months. All requests require an itemized budget and must be countersigned by the grantee institution's business office.

Inquiries: Jon Kerner, Deputy Director for Research Dissemination and Diffusion, Division of Cancer Control and Population Sciences, phone: 301-594-7294, email: jon.kerner@nih.gov

In Brief:

Anderson, Imperial College To Collaborate On Targets

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the UCLA College," said Chancellor **Albert Carnesale**. "The new UCLA Institute for Stem Cell Biology and Medicine will enable us to continue fostering such interdisciplinary collaborations and to build upon the existing body of knowledge for the benefit of people worldwide." **Owen Witte**, professor of microbiology, immunology and molecular genetics, and a Howard Hughes Medical Institute investigator, will serve as director of the new institute. Proposition 71, passed by 59 percent of California voters last November, will provide $3 billion for stem cell research. A state institute is being formed in Northern California to allocate funding to stem cell scientists. Grant applications will be available in May. A 29-member oversight and governing board will oversee the institute and review requests for funding. . . . **M. D. ANDERSON** Cancer Center and **Imperial College London** are collaborating on a research program to identify molecular targets for cancer diagnosis and treatments. "With the goal of making more rapid progress in cancer diagnosis and treatment, our collaboration will lead to greater insights into the biology of cancer, and help us take advantage of advances in genomics and proteomics to create new diagnostic tests and targeted therapies for cancer," said **John Mendelsohn**, president of M. D. Anderson Cancer Center. Both institutions have invested in technology transfer and collaborative applied research initiatives, he said. The agreement, the first of its kind for M. D. Anderson, is funded in part by the Department for the Trade and Industry UK-Texas Bioscience Initiative, which promotes collaborative research and development in biosciences and related topics between researchers in the UK and the region around Houston. . . . **COLUMBIA UNIVERSITY** Medical Center received a $10 million grant from the Department of Defense to study under-treatment of breast cancer among black women and to better understand disparities in survival rates. **Alfred Neugut**, professor of medicine and epidemiology at Columbia University Medical Center, co-director of the Cancer Prevention Program at NewYork-Presbyterian Hospital/Columbia, is principal investigator of the DOD-funded Breast Cancer Center of Excellence. **Dawn Hershman**, assistant professor of medicine and epidemiology at Columbia's Mailman School of Public Health, director of the Clinical Breast Oncology Program at New York-Presbyterian/ Columbia and the co-principal investigator of the center. The center will be a collaboration of experts from Columbia University College of Physicians and Surgeons, the Mailman School of Public Health at Columbia University, and New York-Presbyterian Hospital, among other institutions. It will be housed at NewYork-Presbyterian Hospital/Columbia University Medical Center. . . . **CITY OF HOPE** Cancer Center has opened a new Division of Cancer Immunotherapeutics & Tumor Immunology. **Andrew Raubitscheck**, director of radioimmunotherapy, serves as chairman of the new division. **Michael C.V. Jensen**, director of pediatric neuro-oncology, was named associate chairman. **Stephen Forman**, chairman of the Division of Hematology & Hematopoietic Transplantation, is director of clinical research. . . . **MULTIPLE MYELOMA** Research Foundation announced the award of three grants worth $400,000 to researchers working to identify and validate molecular targets that have strong therapeutic potential. The three grants were awarded to: **James Bradner**, of Dana-Farber Cancer Institute; **Robert Orlowski**, of the University of North Carolina at Chapel Hill; and **Allan Weissman**, of the NCI Center for Cancer Research. . . . **GYNECOLOGIC CANCER** Education and Awareness Act of 2005, known as "Johanna's Law," was reintroduced by **Reps. Rosa DeLauro, Kay Granger, Darrell Issa** and **Sander Levin**. The legislation would provide for informative programs on gynecologic cancers, and include grants for outreach and education. . . . **FRED ALT**, professor of pediatrics and a Howard Hughes investigator at The Children's Hospital, Boston, completed his term as chairman of the NCI Board of Scientific Counselors, Basic Sciences Subcommittee.

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Business & Regulatory Report

Product Approvals & Applications:

ODAC Votes Against Combidex, Cites Insufficient Clinical Data For Approval

The FDA Oncologic Drugs Advisory Committee March 2 voted 15 to 4 to not recommend approval of Combidex, an investigational molecular imaging agent sponsored by **Advanced Magnetics Inc**. (Amex: AVM) of Cambridge, Mass., and **Cytogen Corp.** (Nasdaq: CYTO) of Princeton. N.J.

The committee cited insufficient clinical data to support a broad indication for use of the agent to differentiate metastatic from non-metastatic lymph nodes across all cancer types, the companies said.

A decision by FDA on Combidex is expected by the FDA-designated

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Oncology Management:

NCCN Updates Lung Cancer Guideline, Adding Alimta For Second-Line Therapy

National Comprehensive Cancer Network of Jenkintown, Pa., has updated the Non-Small Cell Lung Cancer Guideline, adding Alimta (pemetrexed) as an option for second-line therapy.

The panel indicated that the Eli Lilly drug has been shown to be equivalent to Taxotere (docetaxel) in efficacy, but with less toxicity. The panel also added a recommendation for single agent Tarceva (erlotinib) for advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen.

Concurrent chemoradiation therapy was added as a primary treatment option for unresectable stage IIIB disease where effusions are not present. Paraplatin (carboplatin) in combination with Taxol (paclitaxel) was also added as an alternate regimen to existing recommendations for the Platinol (cisplatin) based combination as adjuvant chemotherapy.

In another development, NCCN released chapters 4 and 5 of the NCCN Drugs & Biologics Compendium: Acute Myeloid Leukemia and Chronic Myelogenous Leukemia.

"The NCCN Drugs & Biologics Compendium contains authoritative and definitive information about the appropriate use of drugs and biologics in the care of patients with leukemia--information that decision-makers at insurance and managed care companies and pharmacy benefits managers can use to establish coverage policy," said William McGivney, CEO of the NCCN. "With the release of the leukemia chapters, NCCN utilization information adds to a long list of scientific, evaluative products to facilitate decision-making about appropriate cancer care."

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FDA Approves Phase III Trial For BEMA Fentanyl For Pain

(Continued from page 1)

user fee goal date of March 30, 2005, the companies said.

"We understand the advisory committee's position relative to a broad label for Combidex and remain committed to the ongoing development of the agent," said Jerome Goldstein, chairman, president and CEO of Advanced Magnetics.

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BioDelivery Sciences International Inc. (Nasdaq: BDSI) of Newark, N.J., said FDA has approved the use of its 505(b)(2) regulatory pathway for regulatory approval consideration for the BDSI licensed BEMA fentanyl formulation to enter phase III trials for cancer pain.

"This guidance confirms our evolving development and commercialization strategy of using the FDA's 505(b)(2) approval process to obtain more timely and efficient approval of new formulations of previously approved therapeutics, like fentanyl, which incorporate our licensed drug delivery technologies, such as BEMA," said Mark Sirgo, president and CEO of BDSI. "Because the 505(b)(2) approval process is designed to address new formulations of previously approved drugs, we believe it has the potential to be more efficient and less time consuming than other FDA approval methods."

BEMA fentanyl is a transmucosal formulation of fentanyl, an FDA-approved narcotic pain medication. The formulation uses the patented BEMA technology, originally developed by Atrix Laboratories and exclusively licensed to BDSI in the U.S. through its Arius Pharmaceuticals subsidiary. The BEMA delivery technology consists of a dissolvable, dime-sized polymer disc that is applied to the mucus membrane of the mouth.

The disc dissolves over about 20-30 minutes, delivering the drug across the mucus membrane for rapid absorption and onset of effect, the company said.

BDSI said it is also using the 505(b)(2) approval pathway for its transmucosally delivered formulation of Emezine, an anti-nausea and vomiting medication. BDSI will file an NDA for its formulation of Emezine with FDA in the second quarter of this year.

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Maxim Pharmaceuticals Inc. (Nasdaq: MAXM; SSE: MAXM) of San Diego said Ceplene (histamine dihydrochloride) was granted orphan drug designation by the European Commission acute myeloid leukemia following adoption of a positive opinion by the Committee for Orphan Medicinal Products of the European Agency for the Evaluation of Medicinal Products.

Maxim said it has completed a phase III study of Ceplene + IL-2 (Proleukin) for acute myeloid leukemia in which the treatment group met the primary endpoint of the trial (leukemia-free survival) when compared to the standard of care (no treatment) for subsequent remission in an intent-to-treat analysis, the company said. The treatment group had a significantly better LFS than the control group (P = 0.00964), based on a stratified log-rank test, the company said.

Ceplene is based on the naturally occurring molecule histamine, and prevents or inhibits oxidative stress, protecting immune cells, the company said.

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OSI Pharmaceuticals Inc. (Nasdaq: OSIP) of Melville, N.Y., said the Swiss health authority, Swissmedic, has approved Tarceva (erlotinib) for locally advanced or metastatic non-small cell lung cancer after failure of at least one prior chemotherapy regimen. Tarceva is an oral tablet indicated for daily administration.

As with the U.S. label, Tarceva is indicated for all NSCLC patients after failure of at least one prior chemotherapy regimen and contains no restrictions on its use regarding EGFR status, mutation status, gender, smoking history, histology or ethnicity. OSI was responsible for the U.S. filing of Tarceva in advanced

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NSCLC, which received U.S. FDA approval last November.

In addition, a Marketing Authorization Application was submitted by OSI's European partner Roche to the European Health Authorities last August.

The Swiss health authority's decision to approve Tarceva was based on the pivotal BR.21 study in 731 patients with advanced NSCLC. Tarceva demonstrated a survival benefit in essentially all subsets of patients examined including males and females, patients of Asian and non-Asian origins, patients with adenocarcinoma and squamous cell histology, patients with good as well as impaired performance status and both smokers and non-smokers.

Median and one-year survival of the overall population in the BR.21 study was improved by 42.5 (6.7 versus 4.7 months) and 45 percent (31.2 versus 21.5 percent), respectively, and patients were treated with Tarceva for an average of just over four months in the study (23% of patients were on therapy for more than 6 months). Certain subsets of patients, including never-smokers and patients who had tumors determined to be EGFR positive, were seen to have a large survival benefit in response to treatment with Tarceva, the company said.

The sub-group of patients who never smoked had a substantial survival benefit with a hazard ratio of 0.42. The sub-group of smokers also had a survival benefit (hazard ratio = 0.87) despite the fact that this group was also seen to have a 24 percent higher rate of Tarceva clearance (higher clearance rates lead to lower levels of exposure to drug).

In the pivotal NSCLC trial, the most common adverse reactions in patients receiving Tarceva were rash and diarrhea. Grade three/four rash and diarrhea occurred in nine and six percent of Tarceva-treated patients, respectively. Rash and diarrhea each resulted in discontinuation of one percent of Tarceva-treated patients. Six and one percent of patients needed dose reduction for rash and diarrhea, respectively.

Historically, there have been infrequent reports of serious interstitial lung disease (ILD), including fatalities, in patients receiving Tarceva for treatment of NSCLC or other advanced solid tumors. In the Phase III trial, severe pulmonary reactions, including potential cases of interstitial lung disease, were infrequent (0.8 percent) and were equally distributed between treatment arms. The overall incidence of ILD in Tarceva-treated patients from all studies was approximately 0.6 percent.

Results from two earlier large, randomized, placebo-controlled clinical trials in first-line advanced NSCLC patients showed no clinical benefit with concurrent administration of Tarceva with doublet platinum-based chemotherapy (carboplatin and paclitaxel or gemcitabine and cisplatin) and its use is not recommended in that setting.

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Varian Medical Systems (NYSE: VAR) of Palo Alto said it has received FDA 510(k) clearance for Nasopharynx Applicator Set, a brachytherapy solution for more accurate and flexible treatment of nasopharyngeal cancer.

The applicator set, suitable for use in the nasopharyngeal and oropharyngeal regions, is MR compatible and will be used in combination with external beam radiotherapy, the company said.

Oncology Management:

NCCN Offers Compedium Of Drugs & Biologics

(Continued from page 1)

The NCCN Drugs & Biologics Compendium outlines the appropriate uses of drugs and biologics for cancer patients, as derived from the NCCN Clinical Practice Guidelines in Oncology--recognized and applied nationally as the standard for clinical policy in oncology, network said.

Listed uses include FDA-approved indications as well as those beyond FDA labeling. As with the guidelines, the Compendium spans the continuum of cancer care from early stage to advanced stage disease, and from supportive to palliative care. The Compendium is available at NCCN Drugs & Biologics Compendium at phone 215-690-0254 or at the NCCN Web site www.nccn.org.

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NSI Software Inc. of Palo Alto said **Varian Medical Systems** of Hoboken, N.J., has selected its patented Double-Take software to protect patient information within the Varian VARiS Vision oncology information system.

Double-Take provides oncology departments with continuous protection for critical data in the event of a disaster or system outage, the company said. Regardless of a routine network failure or a catastrophic outage, the oncology department can still access data.

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Solexa Inc. (Nasdaq: SLXA) of Hayward, Calif., said it has completed the genome sequence of the virus Phi-X 174 with its DNA Cluster-SBS technology.

The work demonstrates an end-to-end technology that can sequence human DNA to detect disease-predisposing mutations, the company said. The genome sequence has been repeated a number of times.

While the Phi-X 174 genome sequenced was small at just over 5,000 bases, the amount of sequence data generated was larger, the company said. Whereas conventional DNA sequencing equipment delivers no more than 1,200 bases per sample preparation, the Solexa experiment delivered more than three million bases from a single sample preparation. Thus, sample preparation, which can be a major effort in large-scale DNA sequencing projects, could be reduced by over 1,000-fold, the company said.

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Spectral Genomics Inc. of Houston said it has appointed GE Healthcare as its exclusive international distributor to the research market for its products outside the U.S. and Canada.

Spectral said it would continue to sell its products to clinical diagnostic customers outside North America.

Spectral Genomics develops and manufactures BAC clone microarrays with applications in molecular karyotyping for genetic defects, cancer, and human polymorphisms with further applications in drug discovery and personalized medicine, the company said.

In addition to its 1 mega base resolution SpectralChip 2600 and Constitutional Chip for array CGH, Spectral supplies its proprietary SpectralWare web-based software that automatically processes data produced by microarray laser scanners and displays signals produced from its two dye detection system detecting gains and losses of chromosomal material.

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US Oncology of Houston said has secured a comprehensive strategic alliance agreement with **Northwestern Connecticut Oncology & Hematology Associates** of Torrington, Conn., expanding the member network to more than 900 physicians in over 500 locations in 32 states.

The practice has six physicians, board certified in medical oncology and hematology, in three locations in Torrington, Sharon, New Milford and the surrounding counties, including Eastern New York and Southern Massachusetts.

US Oncology earned $48.1 million on revenues of $2.260 billion for the year ended Dec. 31, 2004. During the previous year, the revenues were $1.966 billion and net income $70.7 million. The company went private last year.

Clinical Trials:

Intarcia Begins Phase III Study Of Combo Hormonal Therapy

Intarcia Therapeutics Inc., of Emeryville, Calif., said it has begun a combined anti-estrogen therapy phase III randomized study of combination hormonal therapy for the first line treatment of advanced breast cancer.

The study objective is to test the hypothesis that the combination of atamestane plus toremifene (Fareston) will be more active than single agent therapy with letrozole (Femara) alone.

"By complementary mechanisms of action, the combination of estrogen receptor blockade and aromatase inhibition addresses both key mechanisms by which estrogen drives breast cancer cell growth," said Alice Leung, CEO of Intarcia Therapeutics. "This offers the opportunity to maximize the effectiveness of hormonal therapy in women with hormone-dependent advanced breast cancer."

"Unlike previous combinations, our approach focuses on selecting the appropriate non-interacting aromatase inhibitor and the estrogen receptor blocker with the least estrogenic activity," said Peter Langecker, chief medical officer and vice president of clinical research at Intarcia Therapeutics. "The start of the CAT study, our second phase III study using combination hormonal therapy, is concurrent with the completion of the enrollment of our first pivotal study."

The study will enroll 420 patients in each of two treatment groups. One group will receive atamestane and toremifene, and the other group will receive letrozole and placebo. The primary goal will be to determine whether the combination therapy will increase the time to disease progression and the rate of objective response when compared to the single agent therapy.

An earlier phase II study showed that atamestane alone is active in postmenopausal women with recurrent hormone dependent breast cancer who had failed previous tamoxifen therapies, the company said. The drug lowered estrogen levels and prevented tumor growth for a median of seven months, suggesting anti-tumor activity. Toremifene was selected by Intarcia as the estrogen receptor blocker to be used with atamestane because it is as active as tamoxifen in first line treatment of metastatic breast cancer and has 40-fold less intrinsic estrogenic activity than tamoxifen, the company said.

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Advanced Viral Research Corp. (OTC Bulletin Board: ADVR) of Yonkers, N.Y., said it has begun a phase II, multi-center trial in the U.S. for AVR118 for

systemic symptoms related to advanced cancers where the patients are not candidates for, or who do not wish to receive, chemotherapy.

The multi-center, randomized, double blind 40-patient study would evaluate the effect of an administered 4.0 ml dose of AVR118 to examine the safety, tolerability and efficacy, the company said.

The drug will be administered for three weeks to compare treatment versus no treatment. Those who did not receive the agent during the first three weeks will be permitted to continue for three weeks. Patients who benefit may be eligible to remain on AVR118, generating longer term safety data, the company said.

AVR118 is a biopolymer with immunomodulator activity, the company said. The peptide-nucleic acid complex, which stimulates the proinflammatory responses required to combat viral infections such as AIDS and human papillomavirus, dampens aberrant autoimmune-type inflammatory responses.

The BRANY network includes: Montefiore Medical Center, Mount Sinai School of Medicine, New York University School of Medicine, North Shore-Long Island Jewish Health System, and Saint Vincent Catholic Medical Centers.

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AmpliMed of Tucson said patient enrollment has begun in a multi-center, phase I/II trial of Amplimexon (imexon inj.), in combination with gemcitabine for untreated advanced pancreatic adenocarcinoma.

The study would determine the maximum tolerated doses of Amplimexon as well as its toxicity in combination with gemcitabin, the company said. Data on tumor response and clinical benefit will also be collected and compared against historical control data in order to help establish the parameters for future clinical development.

The study is conducted at five research sites, including the Anschutz Cancer Pavilion of the University of Colorado Cancer Center and the University of Michigan Cancer Center, the company said.

Amplimexon, imexon injection, a cyanoaziridine compound, attacks cancer cells and avoids bone marrow toxicity and drug resistance by causing the disruption of mitochondria, the energy producing factories of the cancer cell, resulting in the leakage of toxic substances which kill cancer cells, the company said.

"Preclinical findings in models of resistant pancreatic cancer have suggested that the combination of Amplimexon and gemcitabine may be significantly more effective than either drug alone and well tolerated. We are delighted that such prestigious institutions have agreed to participate in this important clinical trial for patients with pancreatic cancer," said Evan Hersh, vice president for clinical affairs and chief medical officer of AmpliMed

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Genetronics Biomedical Corp. (AMEX: GEB) of San Diego said it has begun a phase I trial for pancreatic cancer using its MedPulser Tumor Ablation System. FDA granted the orphan designation for the therapy.

The primary endpoint is to determine the safety profile of the therapy in conjunction with intralesionally-injected bleomycin for unresectable or incurable locally advanced pancreatic cancer, the company said. The secondary endpoints are to assess objective tumor response, patient pain, and weight loss over 24 weeks following electroporation therapy.

"There is typically tremendous pain associated with pancreatic cancer and a lack of good treatment options to control it, leading to very poor quality of life in the final stages of the disease," said Avtar Dhillon, president and CEO of Genetronics. "This study will also exhibit the ability of our electrochemical ablation technique to treat solid tumors inside the body cavity, which may expand the number of solid tumor applications and enhance the market potential of the MedPulser system."

Electroporation therapy using bleomycin has been shown to have anti-tumor activity against resistant human pancreatic adenocarcinoma cells in previous in vitro and in vivo studies, the company said.

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Gloucester Pharmaceuticals Inc. of Cambridge, Mass., said it has received FDA approval, under its special protocol assessment process, to begin a trial of FK228 (depsipeptide), a histone deacetylase inhibitor, for cutaneous T-cell lymphoma.

FK228 was granted the Fast-Track designation as a monotherapy for cutaneous T-cell lymphoma in patients who have relapsed following, or become refractory to, one other systemic therapy, the company said. The product is evaluated in a range of hematologic and solid tumor indications including CL, renal cell carcinoma and hormone refractory prostate cancer in clinical trials sponsored by Gloucester, as well as NCI under a CRADA.

Gloucester said it acquired the rights to FK228 from Fujisawa Pharmaceutical Co, Ltd. in 2004 under an exclusive, worldwide license agreement.

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OSI Pharmaceuticals (Nasdaq: OSIP) of Melville, N.Y., said it has initiated a phase I study of OSI-930, which identifies dual c-kit/VEGFR inhibitors.

A second agent from the program, OSI-817, is being evaluated in pre-clinical toxicology experiments prior to entry into the clinic, the company said. Both the drug candidates are tyrosine kinase inhibitors that block cellular signaling through the receptor tyrosine kinases, c-kit and vascular epidermal growth factor receptor (VEGFR, also known as KDR). The agents target both cancer cell proliferation and blood vessel growth.

The single-center, open-label, vehicle-controlled study of 35 healthy patients in the U.S., would determine the safety and tolerability of single oral doses of OSI-930, the company said. The study will include extensive pharmacokinetic sampling and pharmacodynamic evaluation and would better facilitate the design of clinical program in cancer patients.

Deals & Collaborations:

Adherex, NCI To Enter CRADA For Exherin Development

Adherex Technologies Inc. (AMEX: ADH) (TSX: AHX) of Research Triangle Park said the Developmental Therapeutics Program of the NCI Division of Cancer Treatment and Diagnosis has approved a level III collaboration to develop ADH-1, known as Exherin.

As part of the collaboration, the DTP and Cancer Therapy Evaluation Program will negotiate a CRADA with Adherex for clinical trials and additional preclinical studies of the compound, the company said. The studies will evaluate anticancer and vascular targeting effects of the compound, both as a single agent and in combination with other agents for advanced resistant cancers that express the molecular target N-cadherin.

To date, 57 cycles of ADH-1 have been administered to 41 patients in the ongoing phase I trial, the company said. The drug has been well tolerated at doses of up to 840 mg/m2 and is now being studied at a dose of 1000 mg/m2. Three of 17 patients with tumors that express the molecular target N-cadherin have demonstrated evidence of anti-tumor activity following a single dose of ADH-1.

In January, Adherex said it initiated a phase Ib/II study in Europe, with actives sites in Switzerland and Italy, to investigate a weekly dosing schedule. A second phase Ib/II trial of ADH-1 with a daily x 5 dosing schedule in North America would begin in early 2005. A phase II study would investigate an every three-week dosing schedule of ADH-1 given as a single agent for one of a number of different N-cadherin positive tumor types, the company said.

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Applied Biosystems (NYSE: ABI) of Foster City, Calif., and its partner **MDS Sciex**, a division of MDS Inc. (NYSE: MDZ; TSX: MDS) and **Phenomenome Discoveries Inc**., said they have entered into a collaboration to develop software for metabolomics analysis for certain Applied Biosystems/MDS SCIEX mass spectrometers.

Under the agreement, PDI will customize its proprietary non-targeted metabolomics analysis software for use on Applied Biosystems/MDS SCIEX 4000 Q TRAP and QSTAR XL LC/MS/MS Systems, and will ensure compatibility with Analyst Software, the data acquisition and analysis software for the Applied Biosystems/MDS SCIEX instruments, the companies said. PDI said it would use the systems for sample analysis for both internal research projects and external contract work in conjunction with its analysis software, and provide performance input on the Applied Biosystems/MDS SCIEX mass spectrometry software and hardware platforms.

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BioSeek Inc. of Burlingame, Calif., said it has received a milestone payment in its development collaboration with **Dynavax Technologies Corp.** (Nasdaq: DVAX).

In the collaboration, BioSeek said it has used its proprietary BioMAP Systems to characterize the biological activity of TNF-alpha inhibitors known as thiazolopyrimidines.

Dynavax said it is conducting research on orally available small molecules in this compound class for chronic inflammatory diseases. Under the terms of the agreement, BioSeek is eligible for additional milestone payments and royalties on future product sales.

BioMAP Systems are human cell-based assay systems. In each system, combinations of human primary cells are activated in complex environments, replicating intricate cell and pathway interactions found in human physiology, the company said. Depending on their mechanism of action, compounds induce specific changes in the expression of protein readouts, producing a BioMAP profile.

New BioMAP profiles are benchmarked against a large number of reference profiles in the BioSeek database using proprietary algorithms to characterize drug function, including mechanism of action and secondary or off-target activities, and to provide insights into clinical applications. The drug discovery platform can detect and distinguish mechanistically diverse compound classes, identifying lead compounds.

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Corixa Corp. (Nasdaq: CRXA) of Seattle and **Lorantis** of Cambridge, U.K, said they have entered into a joint collaboration to continue developing a therapeutic hepatitis B vaccine, containing the Corixa RC-529 adjuvant and the Lorantis CV-1831, a hepatitis B core antigen, previously owned by Apovia Inc.

Lorantis said it has acquired the Apovia interest in the hepatitis B vaccine technology and under the terms of the new agreement, the company will assume many of the Apovia development responsibilities. Corixa will take the lead for the regulatory applications and management of all clinical trials. Lorantis will lead the completion of preclinical studies and supply the hepatitis B core antigen.

The companies will share equally in all costs and revenues associated with the development of the vaccine. Following proof-of-principle clinical trials, the companies intend to partner the vaccine to a late-stage development and commercialization organization.

RC-529 is the Corixa lead synthetic adjuvant that can be formulated for a variety of applications including intranasal and pulmonary vaccines, the company said.

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Cytyc Corp. (Nasdaq: CYTC) of Marlborough, Mass, said its acquisition of Proxima Therapeutics Inc. has cleared antitrust review.

Cytic said the companies had entered into a definitive merger agreement in February for the purchase price of $160 million, plus a two-year earnout based on incremental sales growth in breast related products, to be paid out of existing cash. MammoSite Radiation Therapy System, the Proxima lead and proprietary product, is a single-use device that positions radiation sources directly into the post-lumpectomy site to optimize radiation treatment delivery while minimizing damage to healthy tissue.

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Gene Network Sciences of Ithica, N.Y., said it has signed an oncology drug development contract with **Johnson & Johnson Pharmaceutical Research & Development**.

Under the agreement, J&JPRD will use proprietary pathway inference technology and data-driven computer models from GNS to determine the pathways associated with the mechanism of action, biomarkers and tumor specificity of a pre-clinical oncology compound, the company said.

Existing GNS models are customized and enhanced for customers with their compound-specific experimental data, the company said, said Colin Hill, CEO of GNS The models become more robust as GNS uses its proprietary network inference techniques to explore millions of what if hypotheses about the functions of genes and proteins within pathways affected by a compound and infer probable network architectures.

The results are incorporated into mechanistic simulations of cell function and human biology that connect molecular-level interactions to disease phenotypes. The models become increasingly accurate during the iterative process, with inference predicting new genes, proteins and interactions to be included in the simulations, while the simulations test hypotheses and help determine additional experiments.

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Grant Life Sciences Inc. (OTC Bulletin Board: GLIF) of Raleigh, N.C., said it has entered into an agreement with **Allogen Labs**, a wholly owned subsidiary of the Cleveland Clinic Foundation, wherein Allogen will perform testing and validation studies on the GLF protein-based HPV/cervical cancer diagnostic technology and kits.

Under the agreement, Allogen said it would screen pre-cancerous and cervical cancer patient samples with the GLF proprietary test to determine the efficacy of the technology. The test, which consists of synthetic peptides derived from human papillomavirus proteins, would be the first diagnostic to directly detect cervical cancer, the company said.

"The market for cervical cancer testing is enormous, and Allogen Laboratories will aid in the speed and quality of our development plans for our non-invasive, protein-based diagnostic," said Stan Yakatan, chairman and CEO of Grant Life Sciences.

Through a proprietary protein-based technology, the assay would identify cervical cancer, its precursors or the likelihood of its presence, the company said. The immunotest includes antibodies associated with HPV-caused neoplasias or cancers that are detected with synthetic, proprietary peptides or amino acid sequences derived from HPV proteins.

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Locus Pharmaceuticals Inc. of Blue Bell, Pa., said it has entered into a computational-directed research agreement with **Scios Inc**. for protein kinases.

Locus said it uses one of the largest privately-owned supercomputer clusters to identify binding sites on protein targets, generate potent small molecule ligands that bind to the sites, and optimize the compounds for appropriate drug-like properties.

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Pepscan Systems of Lelystad, **ServiceXS** of

Leiden, and **Solvay Pharmeuticals** of Weesp, all of The Netherlands, said they have entered into a research agreement for the de-orphanization of a series of proteases.

Under the collaboration Pepscan and ServiceXS will use their expertise in peptide arrays and peptide micro-arrays to identify peptide substrates for a series of proteases proprietary to Solvay, the companies said. The substrates will be identified using rationally and randomly designed peptide arrays.

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Solexa Ltd. of Cambridge, U.K., and **Lynx Therapeutics Inc.** (Nasdaq: LYNXD) of Hayward, Calif., said their completed business combination transaction, incorporated in Delaware, is named **Solexa Inc**.

Solexa Ltd. has become a wholly owned UK subsidiary. The company has received approval for listing on the Nasdaq SmallCap Market and will begin trading under the symbol SLXA.

John West, CEO of Solexa Ltd., has assumed the CEO position of the combined company, headquartered in California. The board of Solexa Inc. will include members from both companies' pre-closing boards. Craig Taylor, previously the Lynx Therapeutics chairman, will be chairman of the new board.

Solexa Inc. develops and commercializes a platform for genetic analysis, based on Sequencing-by-Synthesis and molecular arrays. The one platform would support many types of genetic analysis, including DNA sequencing, gene expression, genotyping and micro-RNA analysis, the company said. This integration is possible because all are compiled from their fundamental DNA sequences. The technology could generate over a billion bases of DNA sequence from a single experiment with a single sample preparation.

The company said it s long-term goal is to reduce the cost of human re-sequencing to a few thousand dollars, which provide total genetic information on an individual for less than the cost of a scan.

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3M of St Paul, Minn., and **Takeda Pharmaceutical Co. Ltd.** of Osaka, Japan, said they have entered into an exclusive co-development and joint marketing agreement to collaborate on a topical treatment for cervical high-risk human papillomavirus infection and cervical dysplasia.

The compound is in early stage phase I testing, the companies said.

Under the agreement, the companies said they would share further costs of development and then jointly commercialize in the U.S. and the European Union. Takeda will retain exclusive rights in Japan and certain Asian countries, and 3M will have exclusive commercialization rights elsewhere.

The compound, developed by 3M, is part of the family of immune response modifier molecules. 3M markets Aldara (imiquimod) Cream, 5 percent, the first topical IRM to be marketed globally, for actinic keratosis, primary superficial basal cell carcinoma, and external genital and perianal warts.

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Valera Pharmaceuticals Inc. of Cranbury, N.J., said it has entered into an agreement with **BioPro Pharmaceutical Inc.** of San Francisco, providing BioPro with certain exclusive rights in the Asia-Pacific region to develop, distribute and sell Vantas, a 12-month implant for the palliative treatment of advanced prostate cancer.

Utilizing the Valera proprietary Hydron Technology, Vantas delivers an even predetermined dose of histrelin over a 12-month period, the company said. FDA approved the implant in 2004.

Under the agreement, Valera said it received an up-front payment and is entitled to milestones and other fees as well as royalties on future sales. The company will produce product inventory for BioPro for clinical trials while also retaining manufacturing and other production rights relevant to future product sales.

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U.S. Genomics of Woburn, Mass., said it has placed its Trilogy Single Molecule Analyzer at four laboratories: MIT Center for Cancer Research, Massachusetts General Hospital Center for Human Genetic Research, University of Massachusetts Medical School and Rockefeller University.

The platform detects and quantifies individual molecules of DNA, RNA, and proteins, allowing rapid screening of samples rapidly, the company said. The platform combines advances in microfluidics, optical engineering, and labeling strategies to enable genetics, functional genomics, and diagnostics to be performed at the single molecule level.

"We are examining how miRNAs contribute to fundamental cellular biology and essential molecular mechanisms," said Phil Sharp, professor at the MIT Center for Cancer Research. "Classical research tools are sometimes tedious and often sacrifice experimental accuracy. The Trilogy technology uniquely counts individual molecules with lower biological sample requirements, which should allow our researchers to reliably quantitate assays in less time."