THE CANCER LETTER

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Double Trouble For NIH: Democrats Offer Small Increases, Bush May Veto The Bill

By Paul Goldberg

The Democratic majority in Congress had an opportunity to revive support for biomedical research at NIH. However, the appropriations numbers coming from the House and the Senate are causing great frustration among Washington lobbyists. Congress is being anything but generous.

Excluding the proposed $300 million tap for the Global Fund to Fight AIDS, Tuberculosis and Malaria, the House markup gives NIH a 1.9 percent increase from the current year's budget, and the bill that has cleared the Senate committee would provide a 2.8 percent increase.

This is still better than the President's proposal, which is requesting a

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NCI Programs:

Advisors Approve $20.5M Program Of Grants, Contracts For Biospecimen Research

By Kirsten Boyd Goldberg

NCI advisors approved the institute's plan to begin a new program of extramural grants and contracts for biospecimen research.

The $20.5 million biospecimen research program was approved June 28 by the NCI Board of Scientific Advisors.

The biospecimen program will provide $12 million over five years for research contracts, $7.5 million over five years for grants, and a sole source award of $1 million over two years.

Following is an excerpt from the concept statement:

Biospecimen Research to Enable Molecular Medicine. Concept for a new Request for Proposals and a Broad Agency Announcement. Proposed cost for RFP: $3 million per award, four awards distributed over two years, average duration of awards five years. Proposed cost for BAA: $200,000 to $1 million, 10 awards, two to five awards per year, average duration of awards two to five years. Cost of sole source contract: $1 million over two years. Office of Biorepositories and Biospecimen Research, program director: Carolyn Compton.

This concept proposes a program of extramural research to systematically define the impact of key pre-analytical variables in human biospecimens of specific type on downstream molecular data generated from specific molecular analysis platforms, and to develop innovative approaches to the control, monitoring and assessment of biospecimen quality. This research program will fund directed research and development in biospecimen science that

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President Threatens Veto Of Labor, HHS Spending Bill

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nearly 1.7 percent cut, compared to the level approved in the 2007 continuing resolution that set the current NIH budget.

Moreover, it's uncertain whether these modest increases are politically sustainable. President Bush has already said that he would veto the Congressional spending bill for Labor, HHS unless it is substantially trimmed.

Also, an amendment by Sens. Tom Harkin (D-Iowa) and Arlen Specter (R-Penn.) to the Senate committee version of the bill repeals the federal government's restrictions on funding stem cell research. Though a gutsy move, the amendment could trigger a veto.

The report that accompanies the Senate bill indicates that legislators fully understand the consequences of the shrinking NIH budget.

"When the five-year effort to double funding for the NIH ended in fiscal year 2003, few could have imagined that the agency would be in the position it finds itself today," the document states. "After four years of stagnant budgets, its funding has dropped 8.3 percent in real terms. The overall success rate for research project grants stands at just 21 percent. Young investigators have only the slimmest chance of getting approved on their first try, and even some well-established biomedical researchers are leaving the field.

"The impact of this funding squeeze goes far beyond those directly involved in awarding and receiving grants. More importantly, it threatens the pace of biomedical research and could delay cures and treatments that are within reach. And the ripple effect could be felt for decades to come if, as feared, we lose the next generation of scientists to other careers," the report states.

The Senate bill cleared the committee June 21, and the report became available last week. The House bill has gone through markup, but is yet to pass the committee.

"There is a real sense of betrayal," said a Washington lobbyist who asked not to be identified by name. "I've been on conference calls where people are agitated. This was something that the Democrats ran on, and they aren't delivering."

Following the House markup June 21, the Federation of American Societies for Experimental Biology issued a statement that expressed its disappointment with the numbers. "This is the fourth year we've seen a proposal for NIH funding that fails to keep pace with inflation," Leo Furcht, FASEB president, said at the time.

However, the federation appears to have softened its stance, acknowledging that during the current year, Congress had given NIH a $620 million increase instead of a flat budget requested by the President.

"I think the appropriators are doing the best job they can do under these circumstances," said Jon Retzlaff, FASEB's legislative director. "The bigger challenge here is the President's insistence that he plans to veto this bill, which would put any kind of increase in jeopardy."

The Senate committee report directs NCI to conduct research that would eliminate barriers to enrollment in clinical trials.

"This research effort should be undertaken to inform strategies to enhance accrual in cancer clinical trials," the document states. "Current low levels of accrual are often rate-limiting in the development of novel treatment approaches, and solving this problem would ultimately improve outcomes for cancer patients."

In a related development, the report mandates NCI "to provide additional resources to fund clinical trials through the Gynecologic Oncology Clinical Trials Cooperative Group," giving priority to "translational research involving biologic prognosticators and therapeutic effects of chemotherapy."

The report also tells the institute's director "to continue to support a collaborative effort to bring nanotechnology, systems biology and molecular imaging

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together to examine the molecular basis of cancer."

The full text of the NCI section of the Senate report follows:

The committee recommends an appropriation of $4,910,160,000 for the National Cancer Institute. The budget request was $4,782,114,000. The fiscal year 2007 appropriation was $4,797,639,000. The comparable amounts for the budget estimate include funds to be transferred from the Office of AIDS Research.

As explained in the opening section on the NIH, the budget request includes a contribution to the Common Fund equal to 1.3 percent of the Institute's budget. The other amounts above do not include any contribution for the Common Fund.

Blood Cancers. The incidence of lymphoma, multiple myeloma and acute leukemia/myelodysplasia increases dramatically with age, and chronic lymphocytic leukemia is almost exclusively a disease of the aged. The committee urges the NCI to place greater emphasis on translational and clinical research in blood cancers, with particular attention to blood cancers that affect the elderly.

Brain Tumors. The committee strongly encourages the NCI to continue its support for clinical research consortia and SPOREs that focus on brain tumors.

Breast Cancer. The committee again strongly urges the NCI to give increased attention to breast cancer, particularly in the areas of lymphedema, stress, nutrition, exercise, weight, the environment, and ways to help women more fully restore and improve their quality of life after treatment. The committee also urges the NCI to further accelerate advances in breast cancer screening technology and to capitalize on existing and create new technologies that improve early diagnosis, health outcomes, and survival.

Cancer Clinical Trials. Only three percent of adult cancer patients participate in trials, and the participation by senior citizens is even more limited. The committee urges the NCI to support research to investigate decision-making by patients, particularly with respect to barriers to, and decisions on, participation in clinical trials. This research effort should be undertaken to inform strategies to enhance accrual in cancer clinical trials. Current low levels of accrual are often rate-limiting in the development of novel treatment approaches, and solving this problem would ultimately improve outcomes for cancer patients.

Cancer Genome. The committee commends the NHGRI and NCI for launching The Cancer Genome Atlas, which will accelerate the understanding of the molecular basis of cancer using genome analysis technologies, including large-scale genome sequencing, copy number variation, and expression analysis.

Cancer in Minority Communities. The committee commends the NCI for its continuing efforts to establish a cancer center at a minority institution focused on research, treatment, and prevention of cancer in African American and other minority communities.

Cancer in Native Hawaiians. The committee continues to be deeply concerned that mortality rates for all cancers are much higher for Native Hawaiian males and females compared to other residents of the State. The committee strongly urges the NCI to increase research that is focused towards understanding cancer among Native Hawaiians.

Cancer Metastasis to Bone. A frequent complication of cancer is its spread to bone. The committee understands that immune response plays a role in cancer metastasis and urges the NCI to focus research in the emerging area of osteoimmunology. The committee encourages the NCI, NIAMS, NIA, and NIDDK to support research to determine mechanisms to identify, block and treat cancer metastasis to bone. Furthermore, the committee urges the NCI to expand research on osteosarcoma to improve survival and quality of life and to prevent metastatic osteosarcoma in children and teenagers who develop this cancer. In addition, the NCI is encouraged to expand research on tumor dormancy as it relates to bone metastasis.

Communication Research. The committee is pleased to note that the NCI has a long history of supporting research on behavioral and sociocultural influences on cancer outcomes and access to care, including support for communication research to ensure that the public receives accurate, easily understood information about the human papillomavirus vaccine, and thus facilitate access for those who need appropriate care.

Gynecologic Oncology Clinical Trials Cooperative Group. The committee urges the NCI to provide additional resources to fund clinical trials through the Gynecologic Oncology Clinical Trials Cooperative Group. Priority should be given to translational research involving biologic prognosticators and therapeutic effects of chemotherapy to speed the development and delivery of new cancer treatments to women with gynecologic cancers.

HPV Vaccine and Cervical Cancer. The committee urges the NCI to fund research that will allow for the identification of the most cost-effective management strategy for cervical cancer screening in the era of HPV L1 vaccines and to identify the circumstances where Pap

test/HPV screening fails in vaccinated women.

Imaging Systems Technologies. The committee is aware of the potential for improved patient care and disease management represented by molecular imaging technologies, especially positron emission tomography [PET], through its ability to image the biology of many kinds of cancer and other diseases. The committee continues to support the NCI's increased emphasis on examining the molecular basis of disease through imaging technologies such as PET and MicroPET. The committee further encourages the testing of women for breast cancer and men for prostate cancer to demonstrate and quantify the increased diagnostic and staging capabilities of PET relative to conventional diagnostic and staging technologies, including mammography.

Liver Cancer. The committee notes that the incidence of primary liver cancer continues to increase, liver cancer is the only cancer experiencing continuing increases in mortality, and treatment options for physicians remain very limited. Therefore, the committee urges the NCI to work closely with the NIDDK to develop a basic, clinical and translational research program designed to reverse these trends and enhance survivability. In addition, the committee welcomes the conclusions of the October 2006 NCI-Hepatitis B Foundation workshop regarding the early detection of liver cancer, and it urges the NCI to support more work in this area.

Lung Cancer. Lung cancer is the leading cause of cancer death among women and minority populations. The committee encourages the NCI to work with the thoracic surgical community to initiate new clinical trials that involve patients at an early stage of the disease when surgery is a treatment option.

Lymphatic Research and Lymphatic Diseases. The committee urges the NCI to support research on lymphedema and to devote increased resources toward the study of lymphangiogenesis and lymphatic imaging.

Lymphoma Translational and Clinical Research. The committee urges the NCI to capitalize on the recent investment in basic research on lymphoma by aggressively funding translational and clinical research on this disease. The basic research program has resulted in significant information about the biology of lymphoma and better strategies for identifying critical metabolic pathways and immune system functioning in lymphoma. The translational and clinical research effort should be strengthened to accelerate therapeutic development for lymphoma.

Melanoma. The committee commends the NCI for a workshop in February 2007 to develop a Strategic Action Plan for Melanoma Research. The committee strongly encourages the NCI to devote sufficient funds in the areas of research opportunity identified by the plan and issue program announcements in those areas. The committee requests the NCI to report by July 1, 2008, on steps it has taken to implement the plan. In addition, the committee encourages the NCI to support the creation of a Melanoma Investigators Consortium, and to fund a multi-site, multi-year, population-based clinical trial to testy the efficacy of early detection methods. The committee also recommends increased collaboration between the NCI and the NIAMS on their melanoma research activities.

Mesothelioma Research. The committee is concerned with the pace of mesothelimoma research. The NCI is encouraged to establish up to 10 mesothelioma centers and increase related research, including clinical trials, detection and prevention methods, palliation of disease symptoms and pain management.

Nanosystems Biology. The committee encourages the NCI and the Office of the Director to continue to support a collaborative effort to bring nanotechnology, systems biology and molecular imaging together to examine the molecular basis of cancer. Many clinical trials of new drugs are now considered to fail if only 10 percent of patients benefit, yet the 10 percent may represent a specific type of the disease for which the drug may be 100 percent effective. Bringing these three disciplines together may allow researchers to identify specific sub-types of cancer and to better target new interventions. Successful results of such an effort could lead to a molecular classification of many types of cancer and to targeted molecular treatments for molecular-specific diseases.

Neurofibromatosis. Recognizing NF's connection to many of the most common forms of human cancer, the committee encourages the NCI to substantially increase its NF research portfolio in such areas as further development of animal models, natural history studies, genetic and drug screening, therapeutic experimentation, and clinical and pre-clinical and clinical trials. The committee also encourages the NCI to create, fund, and implement NF clinical and pre-clinical trials infrastructures including NF centers, pre-clinical mouse consortiums, patient data bases, and tissue banks. The committee further encourages the NCI to apply existing cancer drugs to NF patients in clinical trials both extramurally and intramurally, and to develop new drugs for NF which could then apply to the general population.

Non-Hodgkin Lymphoma. The incidence rates for non-Hodgkin lymphoma in the general population have doubled since the 1970s, for reasons that are not clear. The committee strongly recommends an enhanced commitment to research focusing on the possible environmental links to lymphoma. The committee suggests that the NCI direct funds to: (1) studies on the identification of environmental-genetic interactions that may influence the development of lymphoma; (2) studies of adequate scope to assure the identification of environmental risk factors for specific subtypes of lymphoma; (3) small studies designed to improve detection and quantification of historically difficult-to-measure environmental factors; (4) studies that are directed toward enhancing the understanding of the role of the immune system in the initiation and progression of lymphoma; and, (5) studies that examine the simultaneous presence of a wide profile of infectious agents among individuals with lymphoma. The committee also notes that lymphoma is often diagnosed in young adulthood and middle age, and survivors may experience immediate, and also late and long-term effects of the disease and treatment. The committee urges the NCI to dedicate some of its survivorship research funds on research issues related to problems confronted by lymphoma survivors.

Ovarian Cancer. The committee urges the NCI to support randomized, prospective studies that would lead to the validation and acceptance of biomarkers for the early detection of ovarian cancer.

Pancreatic Cancer. Research on pancreatic cancer, the country's fourth leading cause of cancer death among men and women, remains underfunded as compared to the top five cancers based on mortality. The committee notes that the NCI currently categorizes grants as falling under a specific cancer type if the grant is at least 25 percent relevant to that cancer. The committee urges the NCI to increase this criterion to 50 percent relevancy for pancreatic cancer research and to fund more pancreatic cancer grants at this higher level so that the minimal dollars being funded toward the disease are truly pushing the research forward. Further, the committee requests that the Institute ensure that pancreatic cancer grants are reviewed by at least three reviewers who are experts in pancreatic cancer research. Finally, the committee is disappointed that the three existing pancreatic cancer Specialized Projects of Research Excellence [SPORE] grants have never been fully funded, and it urges the Institute to fully fund no fewer than three pancreatic cancer SPOREs this year.

Prostate Cancer. The committee commends the NCI for its considerable investment in prostate cancer and encourages the Institute to continue to support research to improve the accuracy of screening and early detection of this disease.

Tuberous Sclerosis Complex. The committee applauds the NCI for supporting a multi-center clinical trial on TSC, and it urges the Institute to support additional clinical trials. The committee also encourages the NCI to continue to support basic research on the mTOR signaling pathway and the role of the TSC1/2 genes in nutrient sensing, insulin signaling and cell growth and proliferation.

The appropriations documents are posted at http://thomas.loc.gov/home/approp/app08.html.

NCI Programs:

Advisors Approve Program In Biospecimen Research

(Continued from page 1)

broadly supports the mission of the NCI.

The program proposes three mechanisms to achieve this goal: an RFP for research studies on multiple, defined pre-analytical variables in normal and cancer tissues and their effects on quality-controlled downstream molecular analysis; a Broad Agency Announcement for research and development in biospecimen quality evaluation and control; and a sole source contract for research on intra-operative ischemia on gene expression and protein analysis.

The combination of RFP and sole-source contract mechanisms proposed above will provide NCI with the desired control over the choice of individual variables to be studied and the platforms for molecular analysis to be used. The BAA mechanism will allow solicitation of innovative approaches to biospecimen quality issues while maintaining control of the direction pursued and the methodology employed. The data produced by this program will be directly applicable to the development of evidence-based approaches to biospecimen collection, processing and storage for NCI-funded research.

NCI research initiatives in cancer genomics, epigenomics, proteomics, and nanotechnology depend on the development of new sources of high-quality human specimens and the identification of appropriate biospecimens in existing resources. Human specimens are essential resources to accelerate the development of molecular-based diagnostics and therapeutics for personalized medicine.

The Office of Biorepositories and Biospecimen Research was established in 2005 to guide, coordinate,

and develop the NCI's human biospecimen resources and capabilities. The research branch of the OBBR, the Biospecimen Research Network, is an essential part of the OBBR's activities and serves to further the OBBR's mission to raise the quality of human specimens for research and emerging personalized medicine through evidence-based approaches.

Information gathered by the NCI in the past five years has identified a significant amount of heterogeneity in the methods used to collect, process, store, and disseminate biospecimens. This heterogeneity affects a number of pre-analytical variables that impact research and development efforts in cancer research. For example, reports in the literature indicate that specific procedural variables (e.g., the length of time between surgical excision and biospecimen freezing, conditions of tissue fixation, blood collection and separation procedures, and sample storage conditions) produce variation in gene expression patterns and detection of protein biomarkers. However, the precise relationships between biospecimen handling and the quality and reproducibility of data for cancer research remain undefined. The lack of information regarding specimen handling variables on molecular testing of human tissues is also problematic in the clinical arena. For example, it is estimated that 20 percent of current HER2 immunohistochemistry testing is inaccurate, at least partially due to variability in tissue fixation and processing conditions.

The significant variances in biospecimen resource practices and protocols for biospecimen handling may affect the outcomes of molecular research initiatives across the cancer research enterprise. Extramural research programs that rely on networks for shared biospecimens, such as the Specialized Programs of Research Excellence and the Early Detection Research Network, are significantly affected by the heterogeneity of human specimens. Private sector efforts to develop cancer diagnostics and therapeutics also are hindered by the difficulties in obtaining high-quality human specimens and developing appropriate, evidence-based biospecimen quality assurance/quality control methods and systems. Large-scale genomic and proteomic studies (e.g., The Cancer Genome Atlas, which focuses on the analysis of DNA and RNA from tumor and patient-matched normal cells, and the Clinical Proteomic Technology Assessment for Cancer project, which addresses the need for reproducibility in technologies for analyzing cancer-relevant proteins and/or peptides in serum and plasma) require sufficient numbers of quality-controlled biospecimens to enable reproducible, statistically significant comparisons of control and research subject samples.

The OBBR has diligently engaged the extramural and intramural research communities in a process to define and prioritize the most important pre-analytical variables and molecular analysis platforms. In July 2005, the OBBR sponsored workshops organized by the trans-NCI Biorepository Coordinating Committee to discuss the state of biospecimen resource operational practices and their impact on research. This workshop was attended by representatives from both the public and private sectors, including biospecimen resource managers, clinicians, pathologists, population scientists, informatics experts, molecular analysis experts, patient advocates, and NCI and NIH staff. The OBBR then sponsored a Biospecimen Research Symposium in early 2006 to identify and prioritize the specific specimen variables that affect molecular analysis results in the translational research community.

In early 2006, the OBBR initiated the Biospecimen Research Network to systematically address the impact of specific variables in individual specimen types on molecular data from given analysis platforms.

Purpose of Concept: The objective of this concept is to request funding to sponsor directed extramural research to (1) systematically assess the effects of human specimen pre-analytical variables on the outcome of genomic and proteomic studies and (2) to develop innovative approaches to the control, monitoring and assessment ofbiospecimen quality. Data resulting from the proposed research program will provide the basis for evidence-based biospecimen protocols that will increase the quality of human specimens for research and emerging personalized medicine.

The research projects will be designed using a transdisciplinary and highly collaborative model, taking into account the many scientific disciplines and operational factors that influence the collection, annotation, processing, and storage of human specimens. The research will be accomplished at multiple sites and supported through contract mechanisms. Research projects will employ a model of controlled and/or well-annotated biospecimen acquisition and molecular analysis.

Proposed Activities Submitted for Approval:

1. RFP for Research Studies in Cancer and Normal Tissue Pre-Analytical Variables: A research contracts mechanism is proposed to address the influence of multiple pre-analytical tissue collection variables on quality-controlled downstream molecular analysis. Contracted hospital centers will collect, under defined experimental protocols, well-annotated and

differentially preserved cancer and normal tissues that will be subsequently sent for molecular analysis at designated SAIC-Frederick laboratories (established for the program through NCI Frederick). A RFP will be issued once per year for the first two years of the five-year program, covering the general areas of research described. Multiple awards may be made each year, with an estimated cost of $12 million over the five-year period of the program. The research studies will be designed to address the effects of multiple pre-analytical variables. Examples may include the following:

—Effects of tissue preservation and processing variables on downstream molecular analysis;

—Effects of post-operative ischemia time on gene expression and protein analysis;

—Determination of optimal tissue preservation conditions for detection of specific clinical, biomarkers in tissues by IHC and/or in situ hybridization (e.g., epidermal growth factor receptor in lung cancer tissues; HER2 in breast cancer tissues);

—Effects of different cancer plasma and serum processing protocols on downstream molecular analysis.

The operational plan for projects is envisioned as follows. Several hospital centers will collect tissues under contract and rigorously document the variables in tissue collection, preservation, and processing procedures applied to those tissues (projected years 1-2). Contractors will be selected based in part on their demonstrated capability to provide biospecimens that are extensively annotated be shipped to central laboratories for molecular analysis. The results of this analysis will begin to define the most important variables for further study. In projected years 3-5 of the project, the hospital centers would be directed to collect tissues under highly specified conditions, and the tissues would be analyzed to determine the most important pre-analytical variables to control for optimal tissue quality for molecular anatysis. The proposed experiments will assess, for example, the impact of tissue preservation methods on cancer tissue analysis using a variety of methods, which may include histology, IRC, in situ hybridization, and various genomic analyses. In summary, an iterative process would be used to collect tissues under specified conditions, analyze the tissues under controlled conditions, and use the results of the analysis to define further experiments. The body of experimental results accumulated under this research program will be used to help promote evidencebased best practices for biospecimen collection, preservation, and processing procedures.

2. BAA Inviting Contract Proposals for Research and Development on Human Biospecimen Quality: The BAA is proposed as a mechanism for inviting contract proposals in several general areas of biospecimen research, described below. A BAA will be issued once per year for five years, covering the general areas of research described. Multiple awards may be made each year, with an estimated cost of $1.5 million per year, for a total cost of $7.5 million over the five-year period. From year to year, the BAA may be modified to add new topics within the general parameters of this concept.

Although the BRN, together with the extramural and intramural communities, already has defined a number of areas for biospecimen research that are critical for the cancer research enterprise, it is essential that additional perspectives be invited to identify and solve the broad range of biospecimen challenges. It is evident, based on discussions held with the extramural community about human specimens, that public and private institutions are struggling within their individual research and development programs to obtain, determine the quality of, and manage biospecimens. Some institutions have successfully developed useful approaches to these problems, but the solutions are not often shared effectively within the research and development community. In addition, there are concerns about the rapid adoption of emerging technologies, including surgical robotics technologies, which may impact the molecular integrity of clinical specimens. Insufficient scientific data are available to the public in these important areas of biospecimen quality.

A primary goal of this initiative is to develop and bring into the public domain the necessary biospecimen QNQC and annotation protocols that must be developed to reproducibly identify cancer biomarkers in tissues, blood and blood products, and bodily fluids. In addition, the effects of emerging clinical technologies on biospecimen quality will be examined. This initiative could, in the future, be complemented with Small Business Innovation Research and Small Business Technology Transfer Program companion mechanisms to engage the private sector biomarker development community in this effort. Areas of interest for proposals may include the following:

—Development of QNQC methods and systems aligned to specific biospecimen types;

—Study of specific plasma and serum processing and storage variables and their effects on downstream proteomics analysis by mass spectrometry;

—Identification and study of intra-operative and post-operative variables affecting prostate and colon

cancer biospecimen quality in robotic versus open surgery;

—Development of annotation systems to document biospecimen collection, processing, and storage variables.

3. Sole Source Contract for Research on the Effects of Intra-operative Ischemia time on Gene Expression and Protein Analysis: A sole source contract is proposed to study the effects of intra-operative ischemia on downstream molecular analysis of metastatic colorectal cancer and normal liver and of primary rectal cancer and normal rectal mucosa. A single, two-year award would be made to Indivumed, GmbH, in the total amount of $1 million.

The proposed study will obtain normal and cancer tissues at the outset of surgery, representing a time zero for intra-operative ischemia, and at prescribed intervals during the surgical procedure. The tissues will be flash frozen and analyzed using protein profiling. cDNA microarray analysis of the same tissues will be performed at the BRN laboratory (SAIC-Frederick).

NCI, NHGRI Award 8 Grants In TCGA Tech Development

As part of The Cancer Genome Atlas pilot project, NIH awarded eight two-year grants totaling $3.4 million to support the development of innovative technologies for exploring the genomic underpinnings of cancer.

NCI and the National Human Genome Research Institute announced the TCGA pilot in December 2005 to test the feasibility of a large-scale, systematic approach to identifying the changes that occur in the genomes of cancer cells. The goal is to generate genomic information that the research community can use to develop new and improved strategies for detecting, treating and, ultimately, preventing cancer.

The types of tumors being studied in the pilot include brain cancer (glioblastoma), ovarian cancer, and lung cancer (squamous cell), which together account for more than 200,000 cases of cancer in the U.S. each year.

"In addition to the detailed genomic data it will generate, there is great hope that TCGA will both advance technological development and drive down its cost," said NCI Director John Niederhuber. "Our greatest challenge will be in applying the volumes of information TCGA will provide about tumors to the genomic data NCI is gathering from large cohorts of patients, in order to better predict, and even prevent, the earliest development of cancer."

"Cancer poses a very complex challenge," NHGRI Director Francis Collins, whose institute led the NIH component of the Human Genome Project. Each of the dozens of types of cancer likely will have a different genomic profile or set of profiles. "We urgently need tools equal to this task. One of the major lessons we learned from the Human Genome Project is that technology development is essential for success."

The institutions and principal investigators chosen to receive the two-year grants are: Baylor College of Medicine, Aleksandar Milosavljevic, $413,000; City of Hope /Beckman Research Institute, Gerd Pfeifer, $465,000; Columbia University, Benjamin Tycko, $443,000; Columbia University, Timothy Bestor, $362,000; Johns Hopkins University, Andrew Feinberg, $464,000; Nimblegen Systems Inc. of Madison, Wisc., Thomas Albert, $415,000; Stanford University, Ronald Davis, $429,000; University of California, Davis, Peggy Farnham, $418,000.

The technology development efforts will influence other key components of the TCGA pilot project: three Genome Sequencing Centers, seven Cancer Genome Characterization Centers, a Data Coordination Center and a Biospecimen Core Resource.

The pilot project will establish a publicly available integrated database that researchers can use to study the genomic changes of specific cancers to develop new targets for a new generation of drugs and diagnostics.

Funding Opportunities:

PA-07-391: Reducing Health Disparities Among Minority and Underserved Children. R21. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-391.html. Inquiries: Shobha Srinivasan, 301-435-6614; ss688k@nih.gov.

PA-07-392: Reducing Health Disparities Among Minority and Underserved Children. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-392.html.

RFP: N02-CM-72401-92: Inbred Rodent Strain Validation and Verification. Response Due Date: July 27. Full text: http://www.fbodaily.com/archive/2007/06-June/16-Jun-2007/FBO-01318749.htm. Inquiries: Patricia White, 301-846-5473.

Clarification: The Lustgarten Foundation for Pancreatic Cancer has clarified an item in the June 15 issue. The foundation is providing $2 million to the Pancreatic Cancer Genome Initiative, which brings the foundation's total overall funding to more than $18 million.

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Business & Regulatory Report

Product Approvals & Applications:

Bayer, Onyx Submit sNDA For Nexavar For Hepatocellular Carcinoma Treatment

Bayer HealthCare Pharmaceuticals Inc. (NYSE: BAY) of Wayne, N.J., and Onyx Pharmaceuticals Inc. (Nasdaq: ONXX) of Emeryville, Calif., announced that a Supplemental New Drug Application for Nexavar (sorafenib) tablets has been submitted to FDA for the treatment of hepatocellular carcinoma.

Nexavar is approved in more than 50 countries for the treatment of advanced kidney cancer. The companies also said that they are planning a company-sponsored phase III study of Nexavar in the adjuvant treatment of HCC following the complete removal of early stage liver cancer.

The sNDA submission is based on positive data from the international,

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Clinical Trials:

Oncolytics Begins Trials Of Reolysin Plus Gemzar For Advanced Cancers

Oncolytics Biotech Inc. (TSX: ONC, NASDAQ: ONCY) of Calgary, Canada, said it has initiated enrolment in its U.K. trial to evaluate the anti-tumor effects of systemic administration of Reolysin in combination with gemcitabine (Gemzar) for advanced cancers including pancreatic, lung and ovarian.

In preclinical studies, the combination of reovirus and gemcitabine has been more effective than gemcitabine or reovirus alone at killing certain cancer cell lines, the company said.

Principal investigators are Johann de Bono of The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research, London, and Jeff Evans of the University of Glasgow and the Beatson Oncology Centre in Glasgow, Scotland, the company said.

The trial, REO 009, has two components. The first is an open-label, dose-escalating, non-randomized study of Reolysin given intravenously with gemcitabine every three weeks. A standard dosage of gemcitabine will be delivered with escalating dosages of Reolysin intravenously. A maximum of three cohorts will be enrolled in the Reolysin dose escalation portion. The second component of the trial will immediately follow and will include a further 12 patients at the maximum dosage of Reolysin in combination with a standard dosage of gemcitabine. The trial is one of three to begin in 2007 that will examine the role of Reolysin in combination with standard chemotherapeutics, the company said.

In another development, the company said patient enrolment

(Continued to page 4)

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FDA Accepts Bristol-Myers' Application For Ixabepilone

(Continued from page 1)

phase III, placebo-controlled Sorafenib HCC Assessment Randomized Protocol (SHARP) trial which demonstrated that Nexavar extended overall survival by 44 percent in patients with HCC (HR=0.69; p=0.0006) versus placebo.

There were no significant differences in serious adverse event rates between the Nexavar and placebo-treated groups with the most commonly observed adverse events in patients receiving Nexavar being diarrhea and hand-foot skin reaction, the companies said. There are no FDA-approved drug therapies that significantly extend survival of patients with liver cancer, the companies said.

"These results are particularly meaningful considering that death rates from liver cancer continue to increase," Susan Kelley, vice president, Therapeutic Area Oncology, Bayer HealthCare Pharmaceuticals, said in a statement. "After more than 100 clinical studies of many agents over three decades, Nexavar is the first drug therapy to demonstrate a significant survival benefit for patients with HCC."

* * *

Bristol-Myers Squibb (NYSE: BMY) of Princeton, N.J., said FDA has accepted for filing and priority review the NDA for the BMS investigational compound ixabepilone, an epothilone B analog.

The proposed indications for the compound are as a monotherapy for metastatic or locally advanced breast cancer after failure of an anthracycline, a taxane, and capecitabine and in combination with capecitabine in metastatic or locally advanced breast cancer after failure of an anthracycline and a taxane.

Ixabepilone inhibits the growth or development of cancer cells, the company said.

* * *

CEL-SCI Corp. (AMEX: CVM) of Vienna, Va., said its cancer drug Multikine has been given Orphan-Drug designation by FDA as a neoadjuvant for squamous cell carcinoma of the head and neck.

The science behind Multikine is based on the premise that a healthy immune system can cure cancer, the company said. Multikine is a mixture of naturally occurring cytokines, substances that regulate the immune system. The Multikine mixture is representative of the mixture of cytokines produced by a healthy immune system, the company said.

The product is the first cancer immunotherapy being developed as a first line treatment, the company said. It is administered prior to any other cancer therapy because that is the period when the immune system can still be fully activated.

* * *

Celgene International Sarl (NASDAQ: CELG) of Boudry, Switzerland, said Revlimid (lenalidomide) has been granted full marketing authorization by the European Commission in combination with dexamethasone for multiple myeloma with at least one prior therapy.

The approval is the first regulatory approval for Celgene in Europe, and Revlimid represents the first breakthrough oral therapy in Europe for multiple myeloma in more than forty years, the company said.

"We are working with local regulatory authorities to determine next steps for pricing, reimbursement and distribution plans for all EU member states so that the drug is available as quickly as possible," said Aart Brouwer, president of Celgene International.

The Marketing Authorization Application for was based upon the safety and efficacy results of two randomized phase III special protocol assessment trials, North American Trial MM-009 and International Trial MM-010, evaluating Revlimid plus dexamethasone for multiple myeloma with at least one prior therapy, the company said.

The drug has obtained Orphan Drug designation in the E.U., U.S. and Australia for multiple myeloma, the company said. Revlimid is approved as an oral

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treatment in combination with dexamethasone by the European Commission, following the recommendation from the European Medicines Agency, and by FDA for multiple myeloma with at least one prior therapy. The agent also is FDA approved in the U.S., but not in the E.U., for transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities by, the company said.

In the E.U., the Marketing Authorization Application for its indication is under review by the EMEA Committee for Medicinal Products for Human use.

Revlimid is an IMiDs compound, a member of a proprietary group of immunomodulatory agents, the company said.

* * *

Chroma Therapeutics Ltd. of Oxford, England, said FDA approved its Investigational New Drug application for CHR-2797, its oral, once-daily experimental cancer therapy.

Chroma said it would initiate a second phase II trial of the agent for non-small cell lung cancer.

The first phase II solid tumor study follows the successful completion of a phase I study with CHR-2797 for advanced metastatic solid tumors.

Data from the study showed one partial responder and six patients with confirmed stable disease of at least three months duration, as assessed using RECIST criteria, out of a total of 41 treated with a variety of doses of the drug, said Andrew Protheroe of the Churchill Hospital, Oxford and study investigator. The drug was well-tolerated and drug exposure was consistent with the proposed once-daily oral dosing.

CHR-2797 inhibits aminopeptidases, has demonstrated preclinical efficacy as a monotherapy and has also shown synergy with leading cancer therapies in cancer cells, the company said.

* * *

GlaxoSmithKline of Philadelphia said its New Drug Application for Oral Hycamptin (topotecan) capsules, for relapsed small cell lung cancer, has been granted Priority Review by FDA.

The application was based on a phase III study comparing Oral Hycamptin plus best supportive care to BSC alone in relapsed SCLC, in addition to two phase II and phase III supporting studies, the company said.

In the phase III study, the drug added to BSC was associated with prolonged survival and improvements in common symptoms found with relapsed SCLC. This was the first randomized study to demonstrate that patients with relapsed SCLC live longer when they are treated with chemotherapy, the company said.

Unlike IV Hycamptin, which requires five consecutive days of intravenous therapy every three weeks, Oral Hycamptin will allow treatment at home. If approved by FDA, the product will be the only oral single- agent chemotherapeutic drug approved for SCLC after failure of first-line therapy, the company said.

"The evaluation of an oral treatment is a crucial step towards helping SCLC patients maintain a higher quality of life," said John Eckardt, director of clinical research for the Center for Cancer Care and Research, St. Louis.

* * *

ImClone Systems Inc. (NASDAQ: IMCL) of New York and **Bristol-Myers Squibb Co.** (NYSE: BMY) said FDA has accepted, for filing and review, a Supplemental Biologics License Application for Erbitux (Cetuximab).

The application seeks to include evidence of improved overall survival in the product labeling for Erbitux in the third- line treatment for metastatic colorectal cancer.

The companies also said the Erbitux sBLA has been granted a priority review. Based on the priority review, the likely FDA action date for the sBLA is early October. If the sBLA is approved, Erbitux would be the only biologic therapy to demonstrate overall survival as a single agent in patients with metastatic colorectal cancer, the companies said.

Results from a large, randomized, multicenter, phase III trial, seeks to update the monotherapy indication to include patients with EGFR-expressing mCRC whose disease has progressed following, or who were not candidates to receive, irinotecan- or oxaliplatin-based chemotherapy, the companies said. The sBLA also seeks to include data on overall survival relative to best supportive care - considered to be all approved palliative therapies designed to alleviate pain and treat other effects caused by advanced colorectal cancer.

For mCRC, Erbitux is indicated as a monotherapy for EGFR-expressing mCRC with an intolerance to irinotecan-based therapy. Erbitux is also approved in combination for EGFR-expressing, mCRC in combination with irinotecan refractory to irinotecan-based chemotherapy; the combination indication would remain unchanged. The indications were approved based on objective response rates, the companies said.

Sanofi-aventis of Bridgewater, N.J., said FDA has

accepted for filing and assigned priority review status to the supplemental new drug application (sNDA) for Taxotere(R) (docetaxel) in combination with cisplatin and fluorouracil for the neo-adjuvant therapy of patients with locally advanced squamous cell carcinoma of the head and neck.

The submission is based on results of TAX 324, a randomized, open-label, international phase III trial that was presented at the American Society of Clinical Oncology annual meeting in 2006, showing a Taxotere-based regimen, versus standard chemotherapy, improved overall survival as part of a sequential treatment plan for locally advanced SCCHN.

All patients entering the study had stage III or IV cancer with no distant metastases. Patients in both treatment groups had tumors of the oral cavity, oropharynx, larynx or hypopharynx that could not be removed, tumors considered operable but unlikely to be cured with surgery, or tumors that could not be removed in order to preserve crucial organs.

Overall survival was significantly improved for patients treated with Taxotere based therapy compared to patients receiving just cisplatin and fluorouracil; the relative risk of death was 30% lower (HR 0.70; p=0.0058), the company said. Patients treated with the Taxotere based therapy had a longer median overall survival of 70.6 months vs. 30.1 months for patients receiving cisplatin and fluorouracil, which represents a 40 month absolute improvement in median OS for patients treated with TPF. At three years, 62% of patients who received TPF were alive compared with 48% of those receiving PF.

* * *

Spectrum Pharmaceuticals Inc., (NASDAQ: SPPI) of Irvine, Calif., said **Pharmion Corp**. (NASDAQ: PHRM) has filed a Marketing Authorization Application to the European Medicines Agency for satraplatin in combination with prednisone for metastatic hormone refractory prostate cancer, which failed prior chemotherapy.

The submission is based the 950-patient double-blind, randomized phase III registrational trial, Satraplatin and Prednisone Against Refractory Cancer, or SPARC, comparing Satraplatin plus prednisone to placebo plus prednisone, the company said.

"Data from the SPARC trial demonstrate Satraplatin lowers the risk of disease progression or death by 33 percent compared to control, including for those previously treated with docetaxel chemotherapy," said Cora Sternberg, chief, Department of Medical Oncology, San Camillo Forlanini Hospital, Rome, Italy, and one of the principal investigators of the SPARC registrational trial. "The encouraging results, together with Satraplatin's manageable side effect profile, suggest that the drug represents an important new therapy option for advanced prostate cancer where chemotherapy has failed."

Satraplatin, an investigational drug, is a member of the platinum family of compounds, the company said. The agent is an orally bioavailable compound and is given as capsules that can be taken at home.

The Oncologic Drugs Advisory Committee will review the NDA in July, and an action from FDA on the application is expected in August, the company said.

* * *

Kinex Pharmaceuticals of Buffalo said it has filed its first Investigational New Drug application with FDA for KX2-391, an internally developed small molecule, oral, anticancer product candidate.

KX2-391 is a selective Src kinase inhibitor that targets the peptide substrate binding site, not the ATP binding site as do all other Src inhibitors commercially available or in development, the company said.

* * *

KV Pharmaceutical Co. (NYSE:KVa/KVb) of St. Louis said it has received FDA Approval to market Ondansetron 4 mg. and 8 mg. Orally Disintegrating Tablets.

The tablets are indicated for the prevention of postoperative nausea and vomiting, as well as nausea and vomiting associated with emetogenic cancer chemotherapy and radiotherapy, the company said.

Clinical Trials:

Phase II Trials Of Reolysin For Advanced Cancers Begin

(Continued from page 1)

has commenced in its U.S. phase II trial to evaluate Reolysin in various sarcomas that have metastasized to the lung.

Patients are being enrolled at the Montefiore Medical Center/Albert Einstein College of Medicine in the Bronx, New York, the University of Michigan Comprehensive Cancer Center in Ann Arbor, and the Cancer Therapy and Research Center, Institute for Drug Development in San Antonio, Texas.

"We are now treating patients with advanced cancers in phase II clinical trials in the U.S. and the U.K., with additional phase II trials expected to begin before the end of the year," Brad Thompson, president

and CEO of Oncolytics, said in a statement.

The trial (REO 014) is a Phase II, open-label, single agent study whose primary objective is to measure tumur responses and duration of response, and to describe any evidence of antitumor activity of intravenous, multiple dose Reolysin in patients with bone and soft tissue sarcomas metastatic to the lung. Up to 52 patients will be enrolled, the company said.

Eligible patients must have a bone or soft tissue sarcoma metastatic to the lung deemed by their physician to be unresponsive to or untreatable by standard therapies. These include patients with osteosarcoma, Ewing sarcoma family tumours, malignant fibrous histiocytoma, synovial sarcoma, fibrosarcoma and leiomyosarcoma.

* * *

Genmab A/S (CSE: GEN) of Copenhagen said it has initiated a phase II 56-patient study of ofatumumab (HuMax-CD20) in combination with cyclophosphamide, doxorubicin, vincristine and prednisone, or CHOP, for untreated follicular non-Hodgkin's lymphoma.

The study is being conducted under the Genmab collaboration with GlaxoSmithKline, the company said.

The open label study will treat two randomized dose groups of 28 patients each and will consist of six infusions of ofatumumab in combination with CHOP, the company said. Each will receive 300 mg of ofatumumab at the first infusion, followed by five infusions of either 500 or 1000 mg of ofatumumab every three weeks, in combination with six cycles of CHOP. Disease status will be assessed at three months following the last treatment and then every three months until month 24, and every six months thereafter until 60 months or initiation of alternative treatment.

The study would determine the efficacy of two dose regimens of ofatumumab in combination with CHOP in untreated follicular NHL, the company said. The primary endpoint is objective response from start of treatment until three months after last treatment assessed according to the standardized response criteria for NHL at 30 weeks.

* * *

Lorus Therapeutics Inc. of Toronto TSX: LOR; AMEX: LRP) said enrollment is underway in a clinical trial for GTI-2040 in acute leukemia and myelodysplastic syndrome.

The study would evaluate the safety and activity of GTI-2040 as a single agent for acute leukemia and MDS, the company said. The effect on leukemic blasts and blood count recovery will be assessed as part of an investigation of the pharmacodynamic and pharmacokinetic effects, dose-response relationships and tolerability of the agent during multiple courses of treatment, the company said.

Mark Kirschbaum, director of new drug development at City of Hope, is conducting the study, which is sponsored by NCI Cancer Therapy Evaluation Program under a clinical trials agreement with Lorus.

Other investigators participating in the study are Yun Yen, also at City of Hope, Joseph Tuscano, of University of California Davis Cancer Center, and Kenneth Foon, of University of Pittsburgh Cancer Institute.

The study complements the ongoing development program with GTI-2040 combined with high dose cytarabine in younger patients with acute myeloid leukemia in which complete responses to the combination were found to correlate with downregulation of R2, the cellular target of GTI-2040, the company said.

GTI-2040, an antisense drug, targets the R2 component of ribonucleotide reductase, which is required for DNA synthesis and cell proliferation, the company said. Through downregulation of R2, the drug has demonstrated antitumor and antimetastatic activity in tumor types in both in vivo and in vitro models and is under study in a multiple phase I/II program.

* * *

Multiple Myeloma Research Consortium of Norwalk, Conn., and **Emory University** of Atlanta said they are collaborating on an a multi-center phase I trial to determine the optimal dose level of Velcade (bortezomib) for Injection, a proteasome inhibitor, in combination with tipifarnib, a first-in-clinic farnesyl transferase inhibitor, for relapsed or refractory multiple myeloma.

The MMRC consists of thirteen academic institutions collaborating on multiple myeloma research. MMRC said it is supporting other clinical trials, including a phase I study of NPI-0052, a proteasome inhibitor, in collaboration with Nereus Pharmaceuticals; a phase I study of TKI258, an FGFR3 (fibroblast growth factor receptor 3) inhibitor, in collaboration with Novartis Oncology; and a phase I study of perifosine, Revlimid, and dexamethasone in collaboration with Keryx Biopharmaceuticals.

The Velcade trial would take place at MMRC member institutions including City of Hope National Medical Center, Emory University, and University of Toronto. Emory University and Dana-Farber Cancer Institute will conduct associated correlative science studies.

"Encouraging pre-clinical data suggest that Velcade in combination with tipifarnib may prove to be more active against multiple myeloma cells than either agent alone," said Sagar Lonial, associate professor of medicine at the Emory University Winship Cancer Institute principal investigator.

* * *

Peregrine Pharmaceuticals Inc. (NASDAQ: PPHM) of Tustin, Calif., said the **Medical University of South Carolina** has begun enrollment in a dose confirmation and dosimetry trial of its tumor necrosis therapy Cotara for glioblastoma multiforme.

The MUSC trial conducted earlier studies of Cotara in GBM that showed signs of anti-tumor activity, including one patient that has survived for six years post-treatment, when most with recurrent GBM live only about a year, the company said.

The study leader is Sunil Patel, clinical chairman of the Department of Neurosciences at MUSC.

Treatment in the open label study will consist of Cotara by convection-enhanced delivery, an NIH-developed technique that delivers the agent to the tumor with great precision, the company said. The objectives are to confirm the maximum tolerated dose; to determine radiation dosimetry; and to assess overall survival, progression free survival and the proportion of patients alive at six months following Cotara administration.

Peregrine said it is working with several of its New Approaches to Brain Tumor Therapy clinical sites in the U.S. and with other centers such as MUSC to ensure completion of the U.S. dose confirmation and dosimetry trial. The design of the new Cotara study is a modified version of the protocol developed for the NABTT program.

Cotara links a radioactive isotope to a targeted monoclonal antibody, the company said. The monoclonal antibody binds to DNA that is exposed only on dead and dying cells. The agent is delivered through convection-enhanced delivery, which directs Cotara to the tumor by using a catheter to bypass the blood brain barrier and target the specific tumor site in the brain. Data from clinical studies demonstrated a 58 percent increase in median survival time in late stage glioblastoma multiforme treated with Cotara, the company said. Marketing Authorization Application Filed for Satraplatin With the European Medicines Agency

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Telik Inc. (NASDAQ: TELK) of Palo Alto, Calif., said FDA has placed a clinical hold on the Investigational New Drug Application for Telcyta (canfosfamide HCl).

The hold was initiated following the presentation of Telcyta phase III trial results, the company said.

Enrollment and additional treatment will stop on Telcyta clinical trials, until FDA releases the clinical hold, the company said. Telik said it would submit additional detailed safety and other information regarding Telcyta and meet with FDA as soon as possible.

The only Telcyta clinical trial that had been open for new patient enrollment is the ASSIST-5 trial of Telcyta plus pegylated liposomal doxorubicin versus PLD alone in second line therapy of platinum refractory or resistant ovarian cancer, the company said. In addition, a small number of patients had continued to receive Telcyta treatment in previously-enrolled clinical trials.

Telcyta is a tumor-activated small molecule product candidate in clinical development for advanced ovarian cancer and non-small cell lung cancer, the company said. A second drug development candidate, Telintra (TLK199), is in clinical development for myelodysplastic syndrome. The product candidates were discovered using the Telik proprietary drug discovery technology, TRAP, which enables discovery of small molecule drug candidates, the company said.

In a related development, the company said FDA has converted the full clinical hold of Telcyta trials to a partial hold.

The action will allows enrollees in the ASSIST-3 and ASSIST-5 trials continued study treatments, including Telcyta in combination with chemotherapy, subject to re-consenting procedures, the company said

A second drug development candidate, Telintra TLK199), is in clinical development for myelodysplastic syndrome, the company said. The Telik product candidates were discovered using TRAP, its proprietary drug discovery technology, which enables the rapid and efficient discovery of small molecule drug candidates, the company said.

* * *

YM BioSciences Inc. (AMEX: YMI)(AMEX: TSX: YM), of Mississauga, Ontario, said it has received a No Objection Letter from Health Canada to initiate a phase II trial investigating nimotuzumab for colorectal cancer with failed previous irinotecan-containing regimens.

Nimotuzumab is a humanized monoclonal antibody that targets the epidermal growth factor receptor.

The single-arm 100-patient trial will consist of treatment of irinotecan plus nimotuzumab, the company said. Equal cohorts investigating two dosing schedules will be enrolled.

Nimotuzumab is approved for sale in India and China as well as Latin American countries for head and neck cancers, the company said. It is different from the other antibodies and small molecules targeting the tyrosine kinase pathway as treatment with the other drugs in this class may result in the debilitating and unpleasant side-effects of severe rash, conjunctivitis, painful paronychial inflammation, hypomagnesemia, diarrhea and constipation. Such side-effects have rarely been reported with nimotuzumab treatment, the company said.

YM BioSciences said it also would also file for trials with nimotuzumab in pediatric pontine glioma, and esophageal cancer.

Deals & Collaborations:

Abbott, Genentech To Develop Two Anti-Cancer Compounds

Abbott (NYSE: ABT) of Abbott Park, Ill, and **Genentech Inc.** (NYSE: DNA) of South San Francisco said they have entered into a global commercial collaboration on the research, development and commercialization of two of the Abbott investigational anti-cancer compounds, ABT-263 and ABT-869.

ABT-263, a Bcl-2 family protein antagonist, restores apoptosis in cancer cells, the companies said. ABT-869, a VEGFR-based multi-targeted kinase inhibitor, suppresses tumor growth by preventing new blood vessel growth and by inhibiting angiogenic signaling pathways. Both compounds are in phase I trials for tumors. Phase II trials for ABT-869 will begin this year, the companies said.

Scientists at the two companies said they would conduct additional follow-on research in the area of Bcl-2 family protein antagonists and VEGFR-targeted kinase inhibitors.

ABT-263 restores programmed cell death by blocking the function of pro-survival Bcl-2 family proteins, the companies said. ABT-263 recently entered phase I trials for lymphomas, chronic lymphocytic leukemia and solid tumors, including small cell lung cancer.

ABT-869 inhibits a set of kinases that are involved in angiogenesis, the companies said. The compound is in phase I trials for tumors.

In another development, **Abbott** and **Caprion Proteomics**, a general partnership wholly owned by **Thallion Pharmaceuticals** of Montreal said they have extended a discovery partnership to investigate human therapeutic antibody targets for oncology using their CellCarta technology platform.

The companies began working together on lung cancer targets three years ago. The extended agreement allows Abbott to retain exclusive rights to 10 targets in lung cancer identified by Caprion for up to two years.

* * *

Coley Pharmaceutical Group Inc. (NASDAQ: COLY) of Wellesley, Mass., said **Pfizer**, its partner, has discontinued the lung cancer development program for PF-3512676, an investigational compound, in combination with cytotoxic chemotherapy.

This includes two phase III trials and two phase II trials, the company said.

A scheduled interim analysis of the phase III trials by an independent Data Safety Monitoring Committee showed that there was no evidence that PF-3512676 produced additional clinical efficacy over that achieved with the standard cytotoxic chemotherapy regimen alone, the company said. The DSMC concluded that the risk-benefit profile did not justify continuation of the trials.

* * *

Diplomat Specialty Pharmacy of Flint, Mich., said it has entered into an agreement with **Oncology Physicians Resources** to form OPRx, a program for managing oral oncology medications.

The program helps to manage patient care, track and collect data needed for cancer treatment in the U.S., the company said.

The alliance will give OPR members access to the DSP Oncology Navigator program, which provides clinical and reimbursement solutions to patients with oncologic and hematologic disorders, the company said.

"Diplomat will be the OPR oral oncology Rx solution," said Mark Neville, vice president of sales and marketing for OPR. "With the high number of new oral therapeutic options that have been FDA approved over the past few years, the Diplomat Oncology Navigator has the resources to help OPR patients and physicians gain access to the needed medications regardless of the changing reimbursement landscape."

OPR consists of 42 practices at 77 sites, mostly in Michigan, representing 100 oncologists, the company said.

* * *

Gene Network Sciences of Cambridge, Mass, said it has entered into a cancer treatment collaboration with **Weill Cornell Medical Center** under which the parties will use the GNS proprietary reverse engineering and forward simulation or REFS software platform to

characterize the synergies between farnesyl transferase inhibitors and taxanes.

"Phase I and II trials have shown that the combination of FTIs and taxanes have clinical activity in taxane-refractory cancer patients," said Paraskevi Giannakakou, principal investigator for the collaboration at Weill Cornell. "Discovering the molecular mechanism of action of this combination will pave the way towards identifying subsets of patients likely to benefit from this drug combination and will assist the rational development of therapeutic strategies able to overcome clinical drug resistance."

* * *

PC Biotech AG (Frankfurt Stock Exchange: GPC; TecDAX index; Nasdaq: GPCB) of Martinsried and Munich said has entered into a license agreement with **Yakult Honsha Co. Ltd.** for satraplatin in Japan.

Under the agreement, Yakult gains exclusive commercialization rights to satraplatin for Japan and will lead in developing the drug, the company said. Yakult would provide an upfront payment of 1.2 billion yen (~$10 million) to GPC Biotech as reimbursement for past satraplatin clinical development expenses. Yakult also would make GPC Biotech additional payments based on the achievement of regulatory filing and approval milestones. GPC Biotech said it would also receive a minimum of 21 percent royalties on sales of satraplatin in Japan.

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Hologic Inc. (NASDAQ: HOLX) of Bedford, Mass., said it has entered into a definitive agreement to acquire **BioLucent Inc**. of Aliso Viejo, Calif., and its MammoPad breast cushion business.

Biolucent said it would spin off its brachytherapy business into a new company. The transaction purchase price will be $70 million, plus a two-year earn out, the company said. The closing consideration will consist of $5 million in cash and an additional $65 million payable, at the election of Hologic, in cash, shares of Hologic Common Stock or a combination thereof. The earn-out, if earned, will be payable in two annual cash installments not to exceed $15 million in the aggregate based upon BioLucent achieving certain revenue targets. BioLucent Inc., is a privately held medical device company.

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iCAD Inc. (NASDAQ: ICAD) of Nashua, N.H., said it has signed a development and distribution agreement with **Agfa**, making the iCAD SecondLook Digital CAD solution available for the Agfa direct digital mammography systems.

Agfa will market and sell the solution globally, focusing on Europe and Asia, the company said. iCAD said it would develop a SecondLook Digital solution customized for the Agfa other market-leading mammography systems.

Using algorithms, the iCAD detection software enables earlier cancer detection with less invasive and more effective treatment options, the company said. The iCAD algorithms can detect up to 72 percent of actionable missed cancers an average of 15 months earlier than mammography alone, the company said.

* * *

Qiagen N.V. (NASDAQ: QGEN; Frankfurt, Prime Standard: QIA) of Venlo, Netherlands, and **Digene Corp.** (NASDAQ: DIGE) of Gaithersburg, Md., said they have entered into a definitive agreement to combine the two companies.

Qiagen said it would acquire 100 percent of the Digene stock for a combination of cash and common stock. The transaction combines the Qiagen portfolio of sample and assay technologies, including a panel of molecular diagnostic tests, with the Digene HPV-targeted molecular diagnostic testing. The combined company will have over $350 million of molecular diagnostics revenues and $800 million in revenues overall in 2008, the companies said.

Under the agreement, the transaction will be effected as an exchange offer, followed by a merger of Digene into a subsidiary of Qiagen.

The stock portion of the consideration will be tax-free to Digene shareholders and Qiagen shareholders will own 78 percent of the combined company on a fully diluted basis, and Digene shareholders will own approximately 22 percent, the companies said..

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Rosetta Genomics (NASDAQ: ROSG) of Rehovot, Israel, said it has signed a licensing agreement with **Rockefeller University** for the therapeutic application of proprietary microRNA genes.

The addition of the viral and human microRNAs to the existing intellectual property estate gives Rosetta Genomics access to over 500 proprietary microRNA drug targets, the company said.

Rosetta Genomics therapeutic development program for hepatocellular carcinoma, conducted in collaboration with Isis Pharmaceuticals Inc. (NASDAQ: ISIS), has identified four microRNAs that when inhibited in vitro lead to a decrease in liver cancer cell proliferation, the company said. The liver cancer program at Rosetta Genomics is being funded in part by the Binational Industrial Research and Development Foundation, the company said.