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NCI's caBIG To Expand To Accomplish Four New Clinical Informatics Projects

By Kirsten Boyd Goldberg

In its report to NCI on restructuring the cancer clinical trials enterprise, the Clinical Trials Working Group recommended that the Institute establish four informatics initiatives:

—A clinical trials database of all NCI-funded clinical trials.

—A national clinical trial information technology infrastructure that is interoperable with NCI's cancer Biomedical Informatics Grid (caBIG).

—Standard case report forms that use common data elements.

—A repository of investigator and site credentials that would be recognized by NCI, industry sponsors, clinical investigators, and clinical trial sites.

The institute's other efforts to improve the clinical trials system will not work without the informatics components, NCI Director John Niederhuber said to the NCI Clinical Trials Advisory Committee earlier this month. "The key to this being successful is our ability to bring the power of data management, computing, and information exchange into this equation," he

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In the Cancer Centers:

Top Officials, Staff, Resign From San Antonio's Institute For Drug Development; U01 At Risk

By Paul Goldberg

A group of physicians, scientists, and administrators earlier this month resigned from the Institute for Drug Development, a unit of the San Antonio-based Cancer Therapy and Research Center.

Departing staff members include:

—Anthony Tolcher, director of clinical research at IDD and the principal investigator on that entity's U01 grant from NCI. His departure could be particularly sensitive, because the U01 grant renewal application is due on March 26.

—Chris Takimoto, director of pharmacology at IDD, and a senior investigator on the grant.

—Amita Patnaik, IDD associate director for clinical research.

—Kyriakos Papadopoulos, senior clinical investigator.

—Aracely Cavazos, director of regulatory affairs.

—Gina Mangold, head of contracting.

—Leslie Smetzer, head of research nursing.

—Theresa Mays, director of experimental drug pharmacy.

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More Clinical Investigators Needed To Participate In caBIG

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said. "We haven't done that at all yet, and we have to do that for this to work."

To implement these initiatives, NCI turned to its informatics guru, Ken Buetow, director of the Center for Biomedical Informatics and Information Technology, who has led the development of caBIG.

Buetow is known for his fast-paced presentations describing how, eventually, everyone will be able to plug their cancer research data into caBIG—"a World Wide Web of cancer" as he calls it—and get information out, interacting with a large network of research tools, databases, institutions, and investigators.

In effect, caBIG will have to get bigger to handle the four new projects, Buetow said at the Jan. 10 meeting of the CTAC. Over the past two years, caBIG has been developing a collection of standards and tools for clinical trials. Now, it will expand to bring in more clinical investigators to help build the new databases, he said.

"We will be re-boarding caBIG while we are currently in flight, with a whole bunch of new passengers," Buetow said.

NCI estimates the clinical trials database alone will cost $13.5 million over five years; the institute budgeted $1.3 million for the project last year, and has on its list of funding priorities another $1.8 million this year, but it's not clear whether the funds will be available. Cost estimates of the other initiatives are not yet available, Buetow said at the meeting.

The new projects will be carried out by leveraging caBIG's existing resources and adding to them as necessary, Buetow said. caBIG works similar to open-source software development. Rather building products from start to finish before releasing them to the public, the open-source model invites anyone interested in a project to work with experts and other users to develop, test, and modify software.

More than 50 NCI-designated cancer centers and more than 30 other organizations are working within several "workspaces" in caBIG to help make data interchangeable throughout the cancer research community. The project began in February 2004 and has developed 27 software products, Buetow said. Also, caBIG works closely with commercial software vendors to make their products "caBIG-compatible," he said.

"What we've been doing is building out modular components, that, in a certain sense are like a Chinese menu where you can construct your own banquet, depending on what your institutional needs are," Buetow said.

The Clinical Trials Management Systems workspace will take charge of the four new initiatives, Buetow said. This federation of informatics experts will be expanded to include clinical investigators from cancer centers, cooperative groups, and other NCI clinical trials programs.

"The strategy in this clinical space is standards, standards, standards," Buetow said. "We recognize that the key way for us to work together as a community is to define how we want to communicate with each other, in terms of standards and common architecture. We're not saying standardization, where everyone has to use exactly the same application. What we're saying is you have to breed a community with a structured collection of information in a defined electronic interface."

Within the CTMS, there is a leadership team, a steering committee, initiative management teams, special interest groups, and task forces. The steering committee includes 16 clinical trialists, 13 informatics experts, two patient advocates, 11 NCI staff members, and one FDA staff member.

Last fall, in preparation for the four new initiatives, caBIG began to inventory the existing clinical trials infrastructure, document the community's requirements, and draft policies and procedures for data access, security, and intellectual property protection, Buetow said.

Key to success of the new initiatives will be the

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participation of clinical investigators in the various committees, special interest groups, and task forces, as well as NCI's new clinical trials oversight committees, the CTAC and the Clinical Trials Operations Committee, he said.

Q & A With Advisory Committee

"I do want to encourage you to ask questions, because this is a very big enterprise, and Ken does it at light speed," James Doroshow, director of the NCI Division of Cancer Treatment and Diagnosis, said to the advisory committee after Buetow's presentation.

CTAC member Peter Adamson, of University of Pennsylvania, asked Buetow when the initiatives would be completed.

"The timeline for the clinical trials database is the one that's got the most concrete deadline that's associated with it," Buetow said. "We are hoping to have that functional in no longer than 36 months. We believe we would have components of that available… in as soon as 12 months."

CTAC member Timothy Rebbeck, of University of Pennsylvania, noted that cancer centers have their own data systems, involving a lot of infrastructure. "Is there a mandate or a minimum set of requirements that institutions or cooperative groups or anybody else is going to be held to?" he asked.

"Certainly there is going to be a mandate that all groups have to report clinical trials information into NCI-designated databases in standard sorts of forms," Buetow said. However, centers don't have to throw out their systems, because caBIG is developing modules that will allow these systems to plug in, he said.

"caBIG doesn't diminish anyone's existing investment," Buetow said. "A cancer center that has an investment has a bridge or path to becoming caBIG compatible. A whole infrastructure that has been created facilitates their legacy investment still being a part of the broader network."

CTAC member Richard Schilsky, chairman of Cancer and Leukemia Group B, said the Clinical Trials Support Unit, under contract with NCI, is developing an electronic data capture system, at the same time that caBIG and FDA are working on aspects of electronic data capture.

"How do we make sure that we harness all of these interests and resources, and avoid redundancy, and come up with a universal electronic data capture system as efficiently as possible?" Schilsky asked.

"caBIG is already working with the cooperative groups in your approach to develop a common electronic data capture system," Buetow said. "One of the ways we do it is to see to it that groups don't work in isolation, and as we generate the technical specifications, as well as the operational characteristics of these particular things, that we are working together as a community to see to it that that doesn't happen."

caBIG tries to make sure that "all the key players are at the table," and will bring any difficult issues to the attention of the CTMS steering committee and the CTAC, Buetow said. "The idea is that, now that we have these governance structures in place and broad community representation, we stop before we build again," he said.

"Most of the cancer centers and cooperative groups already have legacy responsibilities to be reporting key information to the NCI," Buetow said. "In many ways, we will be leveraging the existing capabilities at existing institutions to use their capacity to generate some of this information.

"The incentives [for using caBIG] are that, rather than having different reporting to every different divisional entity to NCI, your clinical trials portfolio is a one-stop shop that you can report your information into, using whatever local dialect you speak most easily.

"The disincentives, I would defer back to my broader NCI senior leadership colleagues," Buetow said.

NIEDERHUBER: "I guess if you want money…."

ADAMSON: "Ken, do you have an estimated cost of migration of existing databases into this?"

BUETOW: "I think that's what we're trying to prevent. At this point, the notion of interoperability piece has not yet had a formal cost projection, because there hasn't been a formal decision on what the strategy is, and that's why we need to get the stakeholders together. The caBIG strategy doesn't require you necessarily to leave legacy infrastructures. In fact, what we put in place are bridges that facilitate you using existing infrastructure and reporting into or connecting to the rest of the infrastructure. I don't want to say there's no cost associated with this path, but the adaptors that we build will be freely distributed. It will just be effort necessary to wire your existing system to those adaptors that make it plug-and-play."

JOEL TEPPER, CTAC member, of University of North Carolina: "You talked a lot about putting stuff in. How about getting stuff out?"

BUETOW: "Key to what we are trying to do with the clinical trials database, and I think one of the organizing principles of what we've created today is

the recognition that this is meant to be a two-way street. In the infrastructure that we are already deploying in a first-generation, .5 generation, infrastructure that is increasingly replacing the CDUS reporting infrastructure that you all are familiar with—that infrastructure not only allows you to put the data in, but see all the data that you put in, and where others choose to share it out. Now we have to deal with intellectual property and a human subjects protection and other components, but where it's chosen to be shared, can actually allow anyone in the community to look at it. So, it's a key principle for the new generation of infrastructure, that it's a two-way street. It's not just a Roach Motel where the data goes in and never comes out."

TEPPER: "So you are developing tools to allow various pieces of the information to come out. How do you make those decisions?"

BUETOW: It's actually really complicated, and one thing we are looking forward to is having further conversations with you on what the technical infrastructure is, how this is supported. But as we designed caBIG to date, it uses what we in the IT world refer to as role-based access. It allows any individual group that submits data to decide who, in what roles, we would share that data with. We have probably one of the most sophisticated infrastructures for dealing with access across a network at this time.

"It's actually pretty cool, even if you are not a propeller-head."

Capitol Hill:

Biomedical Research Absent From State of the Union Speech

By Paul Goldberg

In his State of the Union address Jan. 23, President George W. Bush said nothing about biomedical research.

Advocates of funding for NIH take this omission as a sign that the budget proposal scheduled to be released in mid-February would not include increases for research.

In an open letter that preceded Bush's speech to Congress, former House appropriator John Porter, chairman of the board of Research!America, a Washington group, urged the President to focus on biomedical research.

"The President in his State of the Union speech and 2008 budget proposal has a chance to show real leadership by calling for renewed emphasis on science and research as the future of our economy," Porter said in a letter. "America's economic destiny is, without question, tied to our investment in scientific research. Research offers the promise of better health and of better-paying jobs for a better future. I hope the President will outline a vision to speed the pace of science and better prepare our children for careers in a knowledge-based economy.

"This is a time of unprecedented opportunity for science when the U.S., with our talent pool and research capabilities, could be leading the world in medical and scientific advances," Porter said. "We must boost spending for all science and research, not just certain areas. At stake is our standing in the world and our children's standard of living."

Last week, Bush came to NIH to announce that the number of cancer deaths has declined for two years in a row. After that visit, he received a letter from the American Cancer Society chief executive John Seffrin, reminding him that NCI needs additional funding.

Over the past two years, the institute's budget has dropped by $72 million, and was further reduced by inflation. If the President's address is an indication, researchers have no reason to be optimistic about the fiscal 2008 budget.

The Republican-controlled Congress last year passed only two spending bills, passing a continuing resolution that will expire Feb. 15. Democrats said they plan to fund the rest of the government's activities through a year-long continuing resolution in order to give greater attention to the 2008 budget.

Some Capitol Hill observers expect that Congress would nonetheless put additional funds into the National Science Foundation and the research component of the Department of Energy, two programs that were slated to receive raises in fiscal 2007, before the budget process collapsed.

At a Jan. 24 appearance at a DuPont facility, Bush said that "part of my request to Congress is going to be, we want to put $2.7 billion of your money to help concerns and smart people develop new ways of powering our homes and powering our automobiles."

In the Cancer Centers:

Departing IDD Staff Plan To Join Private Practice

(Continued from page 1)

IDD is an unusually structured institution that has been involved in development of many oncology drugs that were subsequently approved by FDA. Though it is supported by a U01 grant, IDD is the only such program

that operates independently from a university.

With four investigators departing, including the top leadership, IDD will be left with three investigators, one of whom is affiliated with Brooke Army Medical Center.

Sources familiar with the situation said the departing staff members are establishing a private group that would conduct phase I research and would be closely affiliated with South Texas Oncology and Hematology, a private physician group that has for years practiced at CTRC.

Efforts to reach STOH and the departing IDD officials were unsuccessful. A CTRC spokesman said the center's top priority at this time is to minimize disruption to patient care and clinical trials. The spokesman said Karen Fields, the CTRC president and CEO, is working with an internal transition team and was not available for an interview with The Cancer Letter by deadline. Fields also serves as the interim director of IDD.

The resignations were first announced by CTRC management to the editorial board of the San Antonio Express-News earlier this month. "When I came here, I set a very high standard in a very compressed time frame," Tyler Curiel, the director of the San Antonio Cancer Institute, the institution that holds the NCI cancer center grant for CTRC, said to the newspaper at the time. "I knew from Day One that there would be fallout, there would be shake-ups. Of course, we didn't expect this big, this fast."

In the same article, Tolcher spoke for the group of staff members who left: "We love the CTRC, and we passionately care about the Institute for Drug Development and drug development in San Antonio," Tolcher said. "Nonetheless, the decision we made was necessary."

CTRC lost its status as the NCI-designated comprehensive cancer center four years ago, and is now a clinical cancer center.

* * *

DUKE Comprehensive Cancer Center, Duke Institute for Genome Sciences and Policy, and the Multidisciplinary Breast Cancer Program, received a $6.8 million research grant from the U.S. Department of Defense for breast cancer research. The funds will be used to develop genomic tools that will predict which chemotherapies will be most effective in early-stage breast cancer patients based on the patient's own genomic signatures, said **P. Kelly Marcom**, clinical director of the Duke Multidisciplinary Breast Program and principle investigator of the project. "We firmly believe that a global assessment of a patient's breast cancer biology can revolutionize early-stage breast cancer treatment by allowing the design of individualized therapy directed by gene expression signatures," said Marcom. "If successful, the developed signatures could be available in a four-to-five-year time frame." Co-investigators include **John Olson, Anil Potti, Joseph Nevins, Joseph Geradts, Jeffery Marks, Sujata Ghate, Bercedes Peterson**, and **Michael Datto**. . . . **WEBSTER CAVENEE**, director of the Ludwig Institute for Cancer Research and professor of medicine in the cancer biology program at the University of California, San Diego, has been awarded the Albert Szent-Györgyi Prize for Progress in Cancer Research by the National Foundation for Cancer Research. He was honored for his work in tumor suppressor genes. The prize includes a $25,000 honorarium. . . . **GREGORY HANNON**, professor at Cold Spring Harbor Laboratory and a Howard Hughes Medical Institute Investigator, was honored by the National Academy of Sciences with its 2007 Award in Molecular Biology for scientific achievement in molecular biology. He was recognized for the elucidation of the enzymatic engine for RNA interference. The award is supported by Pfizer Inc. . . . **RUSSEL KAUFMAN**, president and CEO of the Wistar Institute, was named chairman of council for extramural grants by the American Cancer Society for a two-year term. . . . **STEPHEN WILLIAMS**, director of the Indiana University Cancer Center, was named associate dean for cancer research at the Indiana University School of Medicine. Williams, the H. H. Gregg Professor of Oncology and professor of medicine, has been a member of the IU faculty since 1978 and led the cancer center since 1992. IUCC was designated an NCI clinical cancer center in 1999. . . . **UNIVERSITY OF NEW MEXICO** Cancer Center opened UNM Cancer Center-South in Las Cruces to provide cancer diagnosis and treatment for residents of southern New Mexico and southwestern Texas, said **Cheryl Willman**, director and CEO of the UNM Cancer Center. The new center is a partnership among the UNM Cancer Center, emorial Medical Center Ikard Cancer Treatment Center, and Radiation Oncology Associates, under the leadership of **Kutub Khan**. . . **M. D. ANDERSON** Cancer Center is collaborating with the Instituto Nacional de Cancerologia in Mexico to expand clinical cancer research, prevention and education. The initial areas of collaboration will be leukemia, breast cancer and epidemiological studies. The agreement would further population-based studies of cancer risk factors among Mexicans and Mexican-Americans, including the Mexican-American Cohort Study underway at M. D. Anderson. The collaboration

establishes a plan for a national Mexican tissue bank, and faculty training and education activities related to breast cancer and leukemia, eventually expanding to include clinical research and translational projects, said **John Mendelsohn**, president of M. D. Anderson. . . . **WAKE FOREST UNIVERSITY** Comprehensive Cancer Center was awarded an NCI Program Project grant to investigate the molecular mechanisms and signal transduction pathways involved in the growth suppression of prostate cancer in diets supplemented with n-3 fatty acids, particularly those found in fish oil supplements, center director **Frank Torti** said. Yong Chen in the Department of Cancer Biology is the principal investigator. . . . **CATHIE CHUNG** was appointed to the breast oncology section of the Division of Medical Oncology and Therapeutics Research at City of Hope. She was assistant clinical professor in the Henrietta Lee Breast Center at the USC/Norris Comprehensive Cancer Center.

Pharmaceutical Industry:

Schering To Pay $435 Million To Settle Federal Charges Over Off-Label Drug Promotion

By Paul Goldberg

Schering Sales Corp. was sentenced for making false statements to FDA regarding its improper drug promotional activity and to the Center for Medicare and Medicaid Services regarding its best price for drugs.

Schering Sales and its parent company will pay a total of $435 million to settle criminal and civil charges stemming from off-label promotion of cancer drugs, inflating prices of drugs and making false statements to federal agencies.

Also, Schering Sales, the subsidiary that was the target of the federal investigation, will pay $180 million to settle the criminal portion of the penalty, and will be barred permanently from participation in federal health care programs. The company was sentenced Jan. 17 by Judge Patti Saris of the U. S. District Court for the District of Massachusetts.

The ban on participation in federal contracts is largely symbolic, because it is limited to the subsidiary Schering Sales and doesn't apply to the parent company or its other units, company officials said. The subsidiary currently has no employees.

The company was sentenced for making false statements to government agencies to hide its illegal off-label promotion of Temodar for use in the treatment of brain tumors and metastases, and Intron A for use in treatment of superficial bladder cancer, and conceal its best price on Claritin RediTabs to avoid playing millions in additional Medicaid rebate liabilities.

According to prosecutors, Schering Sales pleaded guilty to conspiring with others to make false statements to the FDA in response to the agency's inquiry regarding certain illegal promotional activities by sales representatives at an oncology conference.

"Those false statements were designed to reassure the FDA that the promotional activities were isolated and not directed by home office, when in fact, the activities were widespread and part of the national marketing plan," the U.S. Attorney's office for the District of Massachusetts said in a statement. "In addition, Schering Sales sought to falsely lull the FDA into believing that it had taken appropriate steps to reinforce the message with its sales representatives that such promotional activities were prohibited, when in fact, the Schering Sales knew and expected that those activities would continue."

The company said that some of the infractions acknowledged by the company occurred a decade ago, and its current senior management, which took over in 2003, has made "business integrity" a top corporate priority.

NIH News:

NIH Hosts Workshops To Improve Grant Review

The NIH Center for Scientific Review plans to convene six workshops this year to seek advice from scientists and others on the grant application peer review process, particularly to examine the organization of its review groups.

CSR's peer review groups have not been assessed by the scientific community since the NIH Panel on Scientific Boundaries for Review released its reorganization plan seven years ago.

"The rapid evolution and expansion of science has made it much more difficult for our peer review groups to keep pace," CSR Director Toni Scarpa said. "The broad and expert input expected from the Open Houses will help accelerate needed changes at CSR, which will help NIH better advance medical research and serve the American public and all those suffering or at risk who need new treatments, cures, and preventions."

The first Open House Workshop, planned for March 2 at the NIH Natcher Conference Center in Bethesda, will examine the alignment of the neuroscience study sections.

Five more workshops will be convened every

other month in these areas: behavioral and social sciences study sections, disease-based study sections, integrated biological study sections (two workshops), and biomolecular study sections.

Comments from the workshops will be posted online, and all those interested will be encouraged to submit additional comment. Leaders of scientific societies and disease groups are encouraged to attend the workshops. Those interested in attending are asked to submit a registration form at least three weeks prior to the workshop. Online registration forms can be found at www.csr.nih.gov/openhouse. While these are open meetings, scientific societies are asked to limit their participation to one or two representatives.

Information from the workshops will be presented to the NIH Peer Review Advisory Committee.

CSR receives about 80,000 NIH and PHS grant applications a year and assigns them to review groups. CSR recruits about 18,000 outside scientific experts each year for its review groups.

In Brief:

Lutter Replaces Gottlieb As FDA Policy Commissioner

RANDALL LUTTER was appointed acting deputy commissioner for policy at FDA. He replaces **Scott Gottlieb**, who resigned. Lutter joined FDA in 2003 as chief economist in the Office of Planning and most recently was associate commissioner of policy and planning. . . . **LARRY KESSLER** was named chairman of the Global Harmonization Task Force for the next nine months. Kessler, director of the Office of Science and Engineering Laboratories in the FDA Center for Devices and Radiological Health, assumed the chairmanship of the forum of medical device regulators and trade associations in December. GHTF is a voluntary group of representatives of national medical device regulatory authorities and trade associations of medical device manufacturers. Kessler joined FDA in 1995 after a decade with NCI, where he had been chief of the Applied Research Branch. . . . **DAVID ADLER** was named government representative to the American Society of Therapeutic Radiology and Oncology. He was director of government affairs for the American Health Quality Association. Also at ASTRO, CEO **Laura Thevenot** was selected to a three-year term on the board of directors of the National Coalition for Cancer Research. . . . **ALEX'S LEMONADE STAND** Foundation, a charity started by the late **Alexandra Scott**, a young cancer patient, has raised $10 million for childhood cancer research since its inception in 2000 as a front yard lemonade stand, the foundation said. The grants program funds 40 research projects in U.S. hospitals. . . . **CORRECTION**: In the Jan. 19 issue of The Cancer Letter, the affiliation of **Dimitrios Colevas** was incorrectly stated. He is in the Investigational Drug Branch of the NCI Cancer Therapy Evaluation Program.

Obituaries:

CHRISTOPHER J. MICHEJDA, 69, senior investigator and head of the Molecular Aspects of Drug Design Section, Structural Biophysics Laboratory in NCI's CCR, died suddenly on Jan. 9 while participating in an Intramural Scientific Retreat.

Michejda was a professor of chemistry at the University of Nebraska in Lincoln before coming to NCI-Frederick in 1978. He received his Ph.D. in physical-organic chemistry at the University of Rochester and then went on to a postdoctoral fellowship at Harvard University. At CCR, his initial focus on chemical carcinogenesis evolved into drug development; he used his talent in chemistry to find new drugs against cancer and viral diseases.

KATHLEEN A. MCMANUS, 85, a former program analyst at NCI, died Jan. 7 of respiratory failure at Sibley Memorial Hospital in Washington, D.C. She began her 17-year career at NCI as a secretary and rose to program analyst before her retirement in 1984.

Funding Opportunities:

RFAs, PAs Available

RFA-CA-07-033: Innovative Technologies for Molecular Analysis of Cancer. R21. Letters of Intent Receipt Date: Jan. 27, April 29, Aug. 27. Application Receipt Date: Feb. 27, May 29, Sept. 27. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-033.html. Inquiries: Gregory Downing, 301- 496-1550; downingg@mail.nih.gov.

RFA-CA-07-034: Innovative Technologies for Molecular Analysis of Cancer. R33. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-034.html.

RFA-CA-07-035: Application of Emerging Technologies for Cancer Research. R21. Letters of Intent Receipt Date: Jan. 27, April 29, Aug. 27. Application Receipt Date: Feb. 27, May 29, Sept. 27. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-035.html. Inquiries: Gregory Downing, 301- 496-1550; downingg@mail.nih.gov.

RFA-CA-07-036: Application of Emerging Technologies for Cancer Research. R21. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-036.html.

RFA-CA-07-036: Application of Emerging Technologies

for Cancer Research. R33. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-036.html. Inquiries: Gregory Downing, 301- 496-1550; downingg@mail.nih.gov.

RFA-CA-07-037: Innovations In Cancer Sample Preparation. R21. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-037.html. Inquiries: Gregory Downing, 301- 496-1550; downingg@mail.nih.gov.

RFA-CA-07-038: Innovations In Cancer Sample Preparation. R33. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-038.html.

RFA-CA-07-039: Innovative Technologies for Molecular Analysis of Cancer. SBIR [R43/R44]. Letters of Intent Receipt Date: Jan. 27; April 29; Aug. 27. Application Submission/Receipt Dates: Feb. 28; May 30; Sept. 28. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-039.html. Inquiries: Gregory Downing, 301- 496-1550; downingg@mail.nih.gov.

RFA-CA-07-040: Innovative Technologies for Molecular Analysis of Cancer. SBIR [R41/R42]. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-040.html.

RFA-CA-07-041: Application of Emerging Technology For Cancer Research. SBIR [R43/R44]. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-041.html. Inquiries: Gregory Downing, 301- 496-1550; downingg@mail.nih.gov.

RFA-CA-07-042: Application of Emerging Technology For Cancer Research. SBIR [R41/R42]. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-042.html.

RFA-CA-07-043: Innovations In Cancer Sample Preparation. SBIR [R43/R44]. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-043.html. Inquiries: Gregory Downing, 301- 496-1550; downingg@mail.nih.gov.

RFA-CA-07-044: Innovations In Cancer Sample Preparation. SBIR [R41/R42]. Full text: http://www.grants.nih.gov/grants/guide/rfa-files/RFA-CA-07-044.html.

PA-07-272: Understanding and Treating Ataxia-Telangiectasia. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-272.html. Inquiries: Richard Pelroy, 301-496-9326; pelroyd@mail.nih.gov.

PA-07-273: Understanding and Treating Ataxia-Telangiectasia. R21. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-273.html.

PA-07-274: Understanding and Treating Ataxia-Telangiectasia. R03. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-274.html.

PA-07-277: Research On Ethical Issues In Human Subjects Research. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-277.html. Inquiries: Kim Witherspoon, 301-496-8866; withersk@ctep.nci.nih.gov.

PAR-07-270: Nanoscience and Nanotechnology in Biology and Medicine. R01. Application Submission/Receipt Date: Feb. 20, June 20, Oct. 22. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PAR-07-270.html. Inquiries: Piotr Grodzinski, grodzinp@mail.nih.gov.

PAR-07-271: Nanoscience and Nanotechnology in Biology and Medicine. R21. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PAR-07-271.html.

PA-07-282: Mechanisms, Models, Measurement, & Management in Pain Research. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-282.html. Inquiries: Ann O'Mara, 301-496-8541; omaraa@mail.nih.gov.

PA-07-292: Research on Social Work Practice and Concepts in Health. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-292.html. Inquiries: Sabra Woolley, 301-435-4589; woolleys@mail.nih.gov.

PA-07-295: Information Technologies and the Internet in Health Services and Intervention Delivery. R01. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-295.html. Inquiries: Audie Atienza, 301-402-8426; atienzaa@mail.nih.gov.

PA-07-297: NIH Pathway to Independence Award. K99/R00. Full text: http://www.grants.nih.gov/grants/guide/pa-files/PA-07-297.html. Inquiries: David Eckstein, 301-496-8580; eckstein@mail.nih.gov.

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Business & Regulatory Report

Product Approvals & Applications:

European Commission Approves Sutent For Advanced Renal Cell Carcinoma

Pfizer Inc. of New York said Sutent (sunitinib malate) has received full marketing authorization from the European Commission for advanced and/or metastatic renal cell carcinoma.

The treatment is the first multiple receptor tyrosine kinase inhibitor to be approved in the EU for first-line use in MRCC, the company said.

Sunitinib malate is an oral therapy dual-action multi-targeted drug that inhibits tumor growth and starves the tumor of blood, the company said.

The approval is based on a phase III 750-patient multicenter international

(Continued to page 2)

Clinical Trials:

Lilly Says Enzastaurin Can't Meet Endpoint In Phase III Glioblastoma Trial; Study Closed

Eli Lilly and Co. of Indianapolis said an external data monitoring committee has recommended that the phase III Study Evaluating Enzastaurin in Recurrent Glioblastoma, or STEERING trial, be closed for enrollment.

Results of the planned interim analysis suggested that enzastaurin would not meet the primary endpoint of improvement in progression-free survival over an existing chemotherapy, the company said.

"Given the independently validated response rate of 22-percent in a phase II trial, we plan to thoroughly review the data from the interim analysis and apply the insights learned to the glioblastoma program," said Richard Gaynor, vice president, cancer research and global oncology platform leader for Eli Lilly and Co. "Based on preclinical and clinical evidence, the company also remains fully committed to the continued development of enzastaurin."

The agent is in a phase III trial, currently enrolling patients, as a maintenance therapy for non-Hodgkin's lymphoma as well as in several phase II studies in tumor types including breast, colon, lung, ovarian and prostate cancers, the company said. The other trials are unaffected by the DMC recommendation.

Enzastaurin is a multi-kinase inhibitor which targets selectively the PKCbeta and PI3/AKTsignaling pathways, the company said. By blocking the pathways over-expressed cancers, the agent suppresses tumor cell proliferation, induces tumor cell death and inhibits tumor-induced angiogenesis.

The STEERING trial is a randomized, open label registration study comparing the efficacy and safety of enzastaurin, taken orally, versus CeeNU (lomustine). The primary endpoint is improvement in progression-free survival.

* * *

(Continued to page 3)

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Tentative FDA Approval For Barr's Generic Kytril

(Continued from page 1)

study in which treatment consisted of sunitinib malate or interferon-alfa, the standard of care, the company said.

Treatment with sunitinib malate had prolonged progression-free survival in first-line treatment with MRCC, the company said. The sunitinib malate arm experienced 11-month median PFS—more than double the 5-month median PFS observed with IFN alfa. Sunitinib malate demonstrated a 5-fold higher objective response rate compared with IFN alfa—28 percent vs. 5 percent. The drug is generally well tolerated with fewer discontinuations than IFN alfa. Fewer patients discontinued the medicine because of treatment-related adverse events—6 percent vs. 9 percent, the company said.

"Doubling median progression-free survival compared to the standard treatment is a promising result," said Sylvie Negrier, deputy director of the Centre Leon Berard, Lyon.

* * *

Barr Pharmaceuticals Inc. (NYSE: BRL) of Woodcliff Lake, N.J., said its subsidiary, Barr Laboratories Inc., has received tentative approval from FDA for its generic version of the Roche Laboratories drug Kytril (granisetron hydrochloride) Tablets, 1mg.

Final approval should come following the expiration of the Roche patent in 2007, or the following year, if Roche seeks and is granted pediatric exclusivity, the company said.

The tablets are indicated for nausea and vomiting associated with emetogenic cancer therapy, including high-dose cisplatin; and, nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation, the company said.

* * *

Bradmer Pharmaceuticals Inc., of Toronto said it has received FDA guidance for its multi-center phase III trial of Neuradiab for newly diagnosed glioblastoma multiforme, which was presented at an end of phase II meeting in November.

"Bradmer received excellent guidance that would finalize the Neuradiab protocol and move the study from Duke University Medical Center to the multi-center trial that would support registration of the therapy," said Alan Ezrin, chief operating officer of Bradmer.

At the meeting, Bradmer said it presented the experience of 200 patients with Neuradiab, plans for the proposed phase III trial, and an outline of the manufacturing program covering the transfer and validation of the drug production from DUMC to commercial manufacturers.

Guidance from FDA included simplifying and strengthening the study design and the agreement to use an exploratory genomic marker to learn about response or failure to respond to conventional chemotherapy, the company said.

The standard of care arm would consist of surgery to remove resectable brain tumor, conventional external beam radiation therapy, and oral temozolimide. The experimental arm would be the conventional standard of care plus a patient specific, single dose of Neuradiab following surgery. The agreed to primary endpoint is median overall survival comparing populations receiving standard of care and standard of care plus Neuradiab, the company said.

Bradmer said it would submit requested materials, including the final protocol, updated manufacturing data, and other related materials to FDA in the first and second quarters of 2007. The company said it would then initiate a multi-center phase III trial .

Neuradiab is a monoclonal antibody conjugated to radioactive iodine that delivers tumor-killing radiation to residual brain tumor cells after surgery, with minimal impact on normal brain tissue, the company said.

* * *

Celgene Corp. (NASDAQ: CELG) of Summit, N.J., said it has been notified of an Abbreviated New

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Drug Application filed with FDA, with a Paragraph IV certification, by Barr Pharmaceuticals Inc. , for thalidomide.

The applicant seeks authorization to market a generic version of thalidomide 100 mg and 50 mg tablets in the U.S. for the acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum, the company said.

Celgene Corp. markets thalidomide under the brand name Thalomid and has marketing approval as a treatment in combination with dexamethasone for newly diagnosed multiple myeloma, as well as for the acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum and as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence, the company said.

Celgene said it would file a complaint alleging infringement of Celgene patents, within the required forty-five day response period.

* * *

Dendreon Corp. (NASDAQ: DNDN) of Seattle said FDA has accepted for filing and has assigned priority review status to a Biologics License Application for Provenge (sipuleucel-T), its investigational active cellular immunotherapy for asymptomatic, metastatic, androgen-independent prostate cancer.

The BLA submission is based on an improvement in overall survival observed in Study D9901, a multi-center, randomized, double-blind, placebo-controlled phase III study, the company said.

Provenge is the first in a new class of active cellular immunotherapies that stimulate the immune system, the company said. In clinical studies, treatment consists of three infusions over a one-month period as a complete course of therapy.

* * *

Ortho Biotech Products, L.P., of Bridgewater, N.J., said FDA has accepted its Supplemental New Drug Application for Doxil (doxorubicin HCl liposome injection) as combination therapy with Velcade (bortezomib) injection for multiple myeloma with at least one prior therapy.

The application was based on a planned interim analysis from the Doxil-MMY-3001 trial, an international, multicenter, phase III, randomized, open-label 646-patient study for relapsed or refractory multiple myeloma with at least one prior line of therapy, the company said. The two treatment groups were randomized to receive Velcade alone dosed at 1.3 mg/m2 intravenously on days one, four, eight, and eleven of a 21-day cycle or Velcade at the same dose plus Doxil 30 mg/m2 given intravenously on day four of the Velcade cycle combination.

The combination of medications provides a nearly three-month improvement in time to disease progression for relapsed/refractory multiple myeloma versus Velcade alone, the company said.

In the study, treatment with a combination of Doxil and Velcade resulted in a 45 percent less risk disease progression and a statistically significant improvement in median TTP, the company said. An independent data monitoring board conducted the interim analysis and determined the TTP was met. As a result, patients still receiving Velcade were offered the addition of Doxil to their regimen, the company said.

* * *

Pharmacyclics Inc. (NASDAQ: PCYC) of Sunnyvale, Calif., said it has submitted a New Drug Application to FDA for Xcytrin (motexafin gadolinium) Injection with FDA to market the drug for non-small cell lung cancer with brain metastases.

The NDA data packet includes efficacy and tolerability data from two phase III randomized, controlled trials of 805 patients, which compared the safety and efficacy of whole brain radiation therapy alone to WBRT plus Xcytrin, the company said. The studies utilized a clinical benefit endpoint that measured neurologic outcomes.

Xcytrin concentrates in tumors and induces apoptosis, the company said. The agent is a redox-active drug that disrupts redox-dependent pathways in cells and inhibit oxidative stress related proteins.

Clinical Trials:

Adventrx Begins Phase II Trial In Metastatic Breast Cancer

(Continued from page 1)

ADVENTRX Pharmaceuticals Inc. (AMEX: ANX) of San Diego said it has begun a phase II trial using CoFactor (ANX-510) for refractory metastatic breast cancer.

CoFactor is a folate-based biomodulator that enhances the activity and reduces associated toxicity of 5-fluorouracil, the company said.

The single arm, 31-patient multicenter study would evaluate the safety and efficacy of CoFactor plus 5-FU in advanced breast cancer where treatment has failed with anthracycline and taxane chemotherapies, the company said. Treatment would consist of CoFactor followed by 5-FU administered by IV bolus weekly for 6 weeks, with tumor and safety assessments every 8 weeks.

The primary endpoint is objective response rate, and secondary endpoints are duration of response, progression free survival, overall survival and incidence and severity of adverse event, as defined by the NCI Common Terminology Criteria, the company said.

* * *

BioCryst Pharmaceuticals Inc. (NASDAQ: BCRX) said it has initiated a trial of its lead oncology drug, Fodosine, for relapsed or refractory T-cell leukemia/lymphoma.

Initiation of the trial triggered $5 million payment from Mundipharma International Holdings Ltd. to BioCryst under the collaboration established last year to develop and commercialize the drug, the company said.

The multicenter, open-label, non-randomized, repeat-dose registration study would be conducted in accordance with a Special Protocol Assessment agreement between FDA and BioCryst and would test a combination of intravenous and oral formulations of the drug, the company said. Designed to determine the rate of complete remission achieved with this regimen of Fodosine, the trial would include sites in the U.S., Eastern and Western Europe, and South America.

Fodosine is being studied in clinical trials for indications including T-cell leukemia cutaneous T-cell lymphoma, B-cell acute lymphoblastic leukemia and chronic lymphocytic leukemia.

Under the partnership, Mundipharma has committed to fund 50 percent of costs, up to $10 million, on trials of the agent to be conducted by BioCryst, as well as an additional $15 million to evaluate the therapeutic safety and efficacy profile of the agent, the company said.

* * *

Biomira Inc. (NASDAQ: BIOM) (TSX: BRA) of Edmonton said it has begun enrollment in a phase II trial of PX-12 for advanced pancreatic cancer.

PX-12, a proprietary small molecule, inhibits the activity of thioredoxin, a protein that regulates cancer-related pathways, the company said.

The randomized, open-label 80-patient trial would evaluate two dose levels of the product for advanced pancreatic cancer where tumors have progressed under treatment with gemcitabine or gemcitabine-containing regimens, the company said. Enrollment would take place at three centers in the U.S.: Virginia G. Piper Cancer Center in Scottsdale; University of Arizona Cancer Center, Tucson; and M.D. Anderson Cancer Center.

The trial is being is partially funding under a Clinical Trials Agreement with the Translational Genomics Research Institute and NCI, the company said. The principal investigator for the trial is Daniel Von Hoff.

In another development, Biomira said the Stimulating Targeted Antigenic Responses To NSCLC, or START Trial, assessing the efficacy and safety of Stimuvax (BLP25 liposome vaccine) for unresectable stage III non-small cell lung cancer is open for enrollment.

The study is being conducted by Merck KGaA of Darmstadt, Germany, and its U.S. affiliate EMD Pharmaceuticals Inc. under the provision of a collaboration agreement between Biomira and Merck, the company said. Biomira said it is entitled to a milestone payment upon enrollment of the first patient in the phase III trial.

Enrollment of 1,300 patients is open to patients in 12 countries, including the U.S., and would expand to additional countries, the company said.

The trial is a randomized, double-blind; placebo-controlled study that would evaluate documented unresectable stage III NSCLC with response or stable disease after at least two cycles of platinum based radio-chemotherapy.

Stimuvax is a vaccine that induces an immune response to cancer cells that express MUC1, a protein antigen, the company said.

* * *

BiPar Sciences Inc. of Brisbane, Calif.**,** said enrollment has begun in its phase Ib study of BSI-201 in cytoxic regimens for solid tumors.

In preclinical studies, BSI-201 a poly-ADP-ribose polymerase, or PARP inhibitor, was shown to induce tumor cell death, the company said. Preclinical studies also suggest the drug is well tolerated and active against a range of tumor types.

The four-arm study is being conducted at three clinical sites: Fox Chase Cancer Center, the Institute for Drug Development of San Antonio and the Barbara Ann Karmanos Cancer Institute, the company said. The company said it began its clinical program last year assessing the agent as monotherapy in an open-label, escalating-dose phase I trial to confirm safety of the drug and establish a maximum tolerated dose and pharmacokinetic profile in solid tumors. That study is being conducted at M.D. Anderson Cancer Center and IDD, is ongoing.

* * *

BN ImmunoTherapeutics Inc. of Mountain View, Calif., said FDA has accepted its Investigational New

Drug Application for MVA-BN-HER2, a breast cancer vaccine. The vaccine would be tested to determine how to incorporate it into standard therapy for metastatic breast cancer, which would include treatment with MVA-BN-HER2 in combination with trastuzumab and chemotherapy, the company said.

* * *

CEL-SCI Corp. (AMEX: CVM) of Vienna, Va., said FDA has approved a phase III study of Multikine for head and neck cancer.

The study would determine the efficacy of the treatment regimen in advanced primary squamous cell carcinoma of the oral cavity, the company said.

The study would test whether the regimen, administered locally prior to the standard therapy for advanced primary squamous cell carcinoma of the oral cavity, would extend overall survival and enhance the local/regional control of the disease, while increasing disease free survival, the company said.

Multikine is a patented immunotherapeutic agent consisting of a defined mixture of naturally occurring cytokines, including interleukins, interferons, chemokines and colony-stimulating factors, the company said.

* * *

CoGenesys Inc. of Rockville, Md., said it has submitted a Clinical Trial Application in Europe of Neugranin, a long-acting form of Granulocyte Colony Stimulating Factor, which is designed to decrease the incidence of infection in myelosuppressive anti-cancer drug treatment.

Pending CTA authorization, the 60-patient phase I/IIa trial would be a randomized, multicenter, double-blind safety and tolerability study for breast cancer, the company said. In the first phase, treatment would be a subcutaneous dose of the drug prior to receiving myelosuppressive chemotherapy (doxorubicin/ Docetaxel). In the second phase, treatment would be chemotherapy prior to dosing with Neugranin, while a positive control group would receive Neulasta, a pegylated form of G-CSF. Evaluations would include safety and tolerability, pharmacokinetic profiles, and, additionally, in the second phase, signals for effect.

* * *

Cytokinetics Inc. (NASDAQ: CYTK) of South San Francisco said NCI has initiated a phase II trial of the kinesin spindle protein inhibitor, ispinesib (SB-715992), as a second-line treatment for renal cell cancer and a phase I trial of ispinesib as a monotherapy in pediatric patients with relapsed or refractory solid tumors.

NCI is sponsoring the trials as a part of a clinical development program to evaluate the safety and efficacy of the drug as monotherapy in multiple tumor types and in combination with other standard chemotherapeutics, the company said.

The open-label phase II study would administer the agent at 7mg/m2 as a one-hour infusion on days 1, 8 and 15 of a 28-day schedule, the company said. In this phase II clinical trial, between 18 and 35 renal cell patients are planned to be treated. The primary endpoint is response rate as determined by the Response Evaluation Criteria in Solid Tumors.

The 30-patient dose-finding phase I study in pediatric patients would investigate the safety, tolerability, and pharmacokinetics and pharmadynamic profile of the product administered as a one-hour infusion on days 1, 8 and 15 of a 28-day schedule, the company said.

Ispinesib has been in a trials program under the sponsorship of GlaxoSmithKline and is also being developed in collaboration with NCI, the company said. Last year, the company said it amended its collaboration and license agreement with GSK. Under the amendment, Cytokinetics said it would assume responsibility for the costs and activities of continued development of the KSP inhibitors ispinesib (SB-715992) and SB-743921, subject to the GSK option to resume responsibility for some or all development and commercialization activities associated with each of the drug candidates.

Cytokinetics said it would conduct a development program for ispinesib to supplement the series of phase I and phase II trials sponsored by GSK that have demonstrated clinical activity metastatic breast and lung cancers and that have shown an acceptable tolerability profile for the agent with standard chemotherapeutics. The program would focus on breast cancer with Cytokinetics incurring $4-7 million of incremental costs in 2007 for clinical development responsibilities under its agreement with GSK.

GSK has sponsored three phase II trials, one evaluating ispinesib as second- or third-line treatment for locally advanced or metastatic breast cancer, one evaluating ispinesib as second-line treatment for non-small cell lung cancer and one evaluating ispinesib as second-line treatment for advanced ovarian cancer, the company said.

In addition, GSK has sponsored three dose-escalating phase Ib trials to evaluate the safety, tolerability and pharmacokinetics of ispinesib in combination with a leading anti-cancer therapeutic, one in combination with carboplatin, the second in combination with capecitabine, and the third in

combination with docetaxel, the company said. The clinical trial evaluating ispinesib in combination with capecitabine is ongoing.

NCI has sponsored five additional phase II trials evaluating the efficacy of ispinesib as a second-line treatment for colorectal cancer, in the first-line treatment of hepatocellular cancer, in the first-line treatment of melanoma, in the first-line or second-line treatment of head and neck cancers, and in the second-line treatment of hormone-refractory prostate cancer, the company said.

NCI has completed enrollment in a phase I trial to evaluate the safety, tolerability and pharmacokinetics of the agent on an alternative dosing schedule for advanced solid tumors that have failed to respond to all standard therapies, the company said. NCI is in enrollment in a phase I trial to evaluate the safety, tolerability and pharmacokinetics of ispinesib on an alternative dosing schedule for acute leukemia, chronic myelogenous leukemia or advanced myelodysplastic syndromes.

* * *

Nuvelo Inc. (NASDAQ: NUVO) of San Carlos, Calif., said it has begun enrollment in a phase II trial for its anticoagulant protein c2 (rNAPc2) in metastatic colorectal carcinoma.

The primary objectives of the multi-center 100-patient, two-stage trial are safety and efficacy of twice-weekly, subcutaneous rNAPc2 for the second-line treatment of mCRC in combination with 5-fluorouracil-based chemotherapy regimens, the companies said. The first stage would evaluate the safety and activity of the agent in a three-tier dose escalation format—2.5, 5, and 10 micrograms/kg. The second stage would include randomizing to doses determined safe during the first stage by an independent Data Monitoring Committee and placebo in conjunction with standard chemotherapy regimens.

* * *

Panacea Pharmaceuticals Inc. of Gaithersburg, Md., said it has begun a prospective multi-center clinical study to evaluate the diagnostic performance of PC Detect, its prostate cancer screening test.

Enrollment is underway at 15 sites in the U.S. to determine if the blood test would detect prostate cancer in men 50 years and older who are referred for biopsy because of a tPSA > 4.0 ng/mL and/or an abnormal digital rectal exam, the company said. The addition of PC Detect to screening methods should reduce the number of prostate biopsies that are subsequently found to be cancer- free.

* * *

Vical Inc. (NASDAQ: VICL) of San Diego said it has begun a phase III trial of Allovectin-7 cancer immunotherapeutic as first-line therapy for recurrent stage III or IV metastatic melanoma.

The trial, known as AIMM (Allovectin-7 Immunotherapeutic for Metastatic Melanoma), would be conducted in accordance with a Special Protocol Assessment at up to 50 clinical sites, the company said. AnGes MG Inc. would fund the clinical trial under a collaborative agreement with Vical.

Because of substantial unmet medical need, the drug has been granted orphan drug designation for invasive and metastatic melanoma by the FDA Office of Orphan Products Development, the company said.

Altogether, 375 patients would be enrolled who may have had surgery, adjuvant therapy, and/or biotherapy, but cannot have chemotherapy, the company said. Randomization would occur on a 2:1 basis: 250 would be treated with Allovectin-7 and 125 would be treated with their physician's choice of either of two chemotherapy agents, dacarbazine or temozolomide. The primary endpoint is a comparison of objective response rates at six months or more after randomization and would also evaluate safety and tolerability as well as survival.

Allovectin-7 is a plasmid/lipid complex containing the DNA sequences encoding HLA-B7 and beta-2 microglobulin, which together form a Class I Major Histocompatibility Complex, or MHC-I antigen, the company said.

* * *

Vicus Therapeutics of Morristown, N.J., said it has received permission from the FDA Division of Oncology Drug Products to proceed with the phase II trial of VT-122 for cachexia in weight losing subjects with stage IV, non-small cell lung cancer.

The trial would be conducted in the U.S. and India, the company said.

The 60-patient multi-center, randomized, open-label controlled study would assess the safety and efficacy of the agent, the company said. Forty would be randomized to receive a defined nutritional support and VT-122 regimen (20 each receiving either of two doses of the first component and individualized maximum tolerated dose of the second component) and 20 receiving only the defined nutritional support. The primary endpoints are maintenance of muscle and muscle function. The study would also measure total body weight and quality of life. Assessments for safety and efficacy would be continued for 12 weeks.

Deals & Collaborations:

Exelixis, Genentech Agree To Co-Develop XL518

Exelixis Inc. (NASDAQ: EXEL) of South San Francisco said it has entered into an agreement with **Genentech Inc.** for the co-development of XL518, a small-molecule inhibitor of MEK.

Exelixis said it has submitted an Investigational New Drug application for the drug to FDA.

MEK, also known as mitogen activated protein kinase, a component of the RAS/RAF/MEK/ERK pathway, is activated in tumors, the company said. Inappropriate activation of the MEK/ERK pathway can promote cell growth in the absence of exogenous growth factors.

Under the agreement, Exelixis said it would receive upfront and milestone payments totaling $40 million upon signing and with the submission of the IND to FDA. Exelixis said it is responsible for developing XL518 through the end of phase I. Exelixis said it has a substantial share in the marketing and commercialization costs, as well as an initial equal share in profits in the U.S., which would decrease as sales increase. Exelixis said it would receive royalties on any sales of the product which may be commercialized outside the U.S.

In another development, Exelixis Inc. said it has begun a phase II trial of XL880 for gastric cancer. In addition, the company said it began a separate phase II trial of XL880 for papillary renal cell carcinoma last year.

XL880 is an orally bioavailable small molecule inhibitor of the MET and VEGF receptor tyrosine kinases involved in tumor cell growth, migration, and angiogenesis, the company said.

The multi-center open-label phase II study would be conducted at multiple clinical sites for poorly differentiated diffuse gastric cancer.

The primary objectives are best-confirmed response rate and safety and tolerability of the drug administered orally for five consecutive days every two weeks. Secondary objectives are progression-free survival, overall survival, duration of response, and to characterize the pharmacokinetic and pharmacodynamic profiles of XL880, the company said.

XL880 targets multiple RTKs implicated in the development, progression, and spread of cancer, the company said. The primary targets of the agent are the hepatocyte growth factor receptor and vascular endothelial growth factor receptor tyrosine kinases, although platelet-derived growth factor receptor, RON, c-KIT, FLT3, and Tie-2 are also inhibited.

In another development, Exelixis Inc. and Bristol-Myers Squibb Co. (NYSE: BMY) said they would enter into a worldwide collaboration to discover, develop and commercialize targeted therapies for cancer.

Under the collaboration, Exelixis would deploy its drug discovery platform and be fully responsible for the identification and pre-clinical development of small molecule drug candidates for mutually selected targets, the companies said. BMS would select up to three Investigational New Drug candidates against three different targets.

BMS said it would pay Exelixis an upfront payment of $60 million in cash. Exelixis would also receive $20 million for each of up to three different drug candidates selected by Bristol-Myers Squibb at IND. The parties plan to share development costs, commercial profits and co-promotion responsibilities in the U.S. Exelixis would receive royalties on product sales outside of the U.S. For each program selected by BMS, Exelixis could opt out of the co-development or co-promotion in the U.S., in which case Exelixis would receive milestones and royalties in lieu of a U.S. profit share.

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Archemix Corp. of Cambridge, Mass., said it has signed a multi-year, multi-target agreement with **Merck KGaA** of Darmstadt, Germany, for discovery, development, and commercialization of first-in-class aptamer-based therapeutics for cancer.

Under the agreement, Archemix would receive an upfront payment and committed research funding of $10 million, the company said.

Aptamers are single-stranded nucleic acids that form well-defined three dimensional shapes, binding target molecules in a manner that is conceptually similar to antibodies, the company said.

* * *

AVEO Pharmaceuticals Inc. of Cambridge, Mass., said it has acquired an exclusive license to develop and commercialize the once-a-day, oral VEGF receptor inhibitor, KRN951, from **Kirin Brewery Co. Ltd.**, in all territories outside of Asia.

KRN951 is completing a 30-patient phase I trial advanced for solid tumors, the company said. Data indicate that seven patients with refractory renal cell carcinoma enrolled to date have achieved either a partial response or stable disease as defined by the trial protocol, with one exhibiting a response lasting more than 2.5 years, said Ferry Eskens, of the Department of Medical Oncology, Erasmus Medical Center of Rotterdam, and lead investigator.

Treatment with the agent was well tolerated, the company said. The most common side effect seen was hypertension. Blood pressure was controlled by standard antihypertensive agents in all but one subject.

AVEO said it would develop KRN951 for renal cell carcinoma, and as a combination treatment in multiple solid tumor types.

"The benefit of VEGF receptor inhibition in multiple tumor types is now well-accepted," said Rick Klausner, former director of NCI and a member of the AVEO scientific advisory board. "Notwithstanding, the field also recognizes that first generation inhibitors may be sub-optimal in important respects."

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GlaxoSmithKline plc (NYSE:GSK) of London said **Pilgrim Acquisition Corp**., its wholly owned subsidiary, is initiating a cash tender offer to purchase outstanding shares of common stock of **Praecis Pharmaceuticals Inc**., (NASDAQ:PRCS), including the associated preferred stock purchase rights, for $5 in cash without interest and less any required withholding taxes.

The offer, which would expire Feb. 6, is being made pursuant to a merger agreement made last year among Praecis, Pilgrim Acquisition Corp., and SmithKline Beecham Corp., a wholly owned subsidiary of GSK, the company said.

In another development, **GlaxoSmithKline** and **Genmab A/S** said they have entered into a worldwide agreement to co-develop and commercialize HuMax-CD20 (ofatumumab), a fully human monoclonal antibody in late stage development for CD20 positive B-cell chronic lymphocytic leukemia and follicular non-Hodgkin's lymphoma and in phase II for rheumatoid arthritis.

Under the agreement, Genmab would receive a license fee of DKK 582 million and GSK would invest DKK 2,033 million to purchase, 4,471,202 ordinary shares of Genmab, the companies said. The value of the agreement in cancer and various autoimmune and inflammatory diseases, could exceed DKK 12.0 billion, including the initial license fee and equity purchase, milestone payments, totaling DKK 9.0 billion and expected development, commercial manufacturing and commercialization costs.

In addition, Genmab would be entitled to receive tiered double digit royalties on global sales of HuMax-CD20, the companies said.

GSK would receive an exclusive worldwide license to HuMax-CD20 as well as other antibodies with affinity for the CD20 antigen which Genmab may develop, the companies said. GSK would also have an exclusive option to a CD20 UniBody to be developed in collaboration with Genmab. GSK and Genmab said they would co-develop HuMax-CD20.

Genmab would be responsible for development costs until 2008, including costs of the two ongoing late stage oncology studies after which development costs would be shared equally. GSK would be solely responsible for the manufacturing and commercialization of HuMax-CD20.

Genmab would have an option to co-promote HuMax-CD20 in a targeted oncology setting in the U.S. and in the Nordic region, the companies said. Should the be undertaken, Genmab would also have the option co-promote Bexxar and Arranon in the U.S. and Atriance in the relevant countries of the Nordic region.

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MaxCyte Inc. of Gaithersburgh, Md., said **Geron Corp.** (NASDAQ: GERN) has exercised an option for a clinical and commercial license to use the MaxCyte proprietary cell loading system in the manufacture of mRNA-loaded autologous dendritic cell-based vaccines, including the Geron GRNVAC1 telomerase vaccine.

The Geron clinical and commercial license to the MaxCyte technology includes a long term supply contract, as well as rights to reference the MaxCyte FDA Master File in the Geron regulatory submissions.

GRNVAC1 is a therapeutic cancer vaccine of autologous dendritic cells loaded ex vivo with telomerase mRNA, the company said.

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Poniard Pharmaceuticals Inc. (NASDAQ: PARD) of South San Francisco and **Scripps Research Institute** said they are expanding their research agreement to include focal adhesion kinase inhibitors for cancer treatment.

The collaboration would be co-led by David Schlaepfer, associate professor, Department of Immunology at Scripps Research Institute, and Chris Liang, director of medicinal chemistry at Scripps Florida.

The initial scientific collaboration was for small-molecule protein kinase inhibitors as therapeutic agents, including cancer treatments, the companies said.

The expanded research by Schlaepfer employs multiple strategies to inhibit FAK activity within tumor cells, the company said. FAK is associated with the invasion and metastasis of tumor cells and has been implicated in chemoresistance, the company said. Inhibitors of FAK may enhance the activity of picoplatin in the treatment of solid tumors.