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NCI Advisors Table Proposed $186 Million Nanotechnology Research Program

By Kirsten Boyd Goldberg

A panel of advisors last week tabled an NCI plan to spend $186.5 million on nanotechnology research over the next five years.

Dealing a setback to the Institute's leadership, the Board of Scientific Advisors June 24 voted unanimously to delay a decision on the Institute's plan to establish an extramural nanotechnology research and training program.

Board members said they had too little time and too little understanding of nanotechnology to comfortably commit funds to the project during a period of flattening of the research budget. The board appointed a subcommittee to further study the proposal and present recommendations to the board at a later date.

NCI officials should have brought in outside experts in nanotechnology

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In Brief:

John Montgomery, Former Panel Member, Developed Anti-Cancer Compounds, Dead

JOHN MONTGOMERY, a member of the President's Cancer Panel from 1983-91, who as an organic chemist with the Southern Research Institute developed anti-cancer compounds, died May 24 at home in Birmingham, Ala. He was 80.

Montgomery, born in Greenville, Miss., attended Vanderbilt University and received a B.A. in chemistry in 1946 and an M.S in organic chemistry in 1947. He received a Ph.D. in organic chemistry from University of North Carolina at Chapel Hill. He began his career with Southern Research Institute in 1952, becoming director of organic chemistry research in 1956, vice president in 1974, senior vice president and director of the Kettering-Meyer Laboratory in 1981, and distinguished scientist in 1990.

Montgomery became affiliated with the University of Alabama at Birmingham Comprehensive Cancer Center in 1978 and was associate director of the UAB Center for AIDS Research from 1988-1994.

He was a founder of BioCryst Pharmaceuticals and served as executive vice president and chief scientific officer from 1990-2002. He served on the BioCryst Board of Directors until May 2004.

In his career, he published over four hundred scientific articles and was awarded 51 patents. From this work have come a number of potential

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Advisors to NCI: Give Us More Time, Background Information

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to make scientific presentations before asking the board to vote on the proposal, advisors said. None of the board members present at the June 24 meeting had seen the proposal more than four days before the meeting.

"To be honest, I simply don't have the knowledge that I would like to have to make a decision about a $186.5 million project," said board member Susan Horwitz, the Falkenstein Professor of Cancer Research at Albert Einstein College of Medicine. "I would like to have had someone stand up here and give a scientific presentation.… We are moving into something that's clearly important, but it's a lot of money at a time when we have a level budget."

Over the past year, several NCI programs ran into problems with advisory boards, at times provoking open, scathing criticism from board members.

—Last fall, BSA similarly tabled an NCI proposal to contract out the tissue banks supported by the clinical trials cooperative groups. The advisory board said the Institute didn't consult the group chairmen, the majority of whom opposed the idea. The board later approved a plan to support the tissue banks through cooperative agreements instead (**The Cancer Letter**, Nov. 21, 2003).

—Earlier this year, the BSA said a $24 million Patient Navigator Program proposed by NCI lacked focus. The board approved the program at the urging of NCI Director Andrew von Eschenbach, but formed a subcommittee to help the Institute rewrite the proposal (**The Cancer Letter**, March 26).

—Earlier this month, Eric Lander, a member of the National Cancer Advisory Board, berated NCI for failure to seek advice from the White House-appointed board before developing plans for a loan program for cancer centers (**The Cancer Letter**, June 18). Lander is director of the MIT Center for Genome Research and member of the Whitehead Institute.

At the June 24 BSA meeting, board members said NCI hadn't made a compelling case for a special program in nanotechnology, and the proposal lacked a mechanism to shut down the program. An Institute of Medicine committee last year recommended that large NIH programs include evaluation components and a phase-out plan (**The Cancer Letter**, June 20, 2003; the report, "Large-Scale Biomedical Science," is available at www.nap.edu).

"I have concerns about investments in building infrastructure," said board member Thomas Curran, chairman of developmental neurobiology at St. Jude Children's Research Hospital, who served on the IOM committee that issued the report. "A great deal of this [NCI proposal] is about building the centers and the infrastructure to coordinate the activities of others. When we discussed this [type of program] on the IOM committee—the 'big science' discussion—we liked the idea that as you initiate a large-scale project like this, you also consider the mechanism for the phase-out of the project."

Other board members were similarly cautious about setting up another large program:

—"I'm not sure I understand the obstacles that are preventing progress in nanotechnology that this strategy seems to resolve," said Robert Young, president of Fox Chase Cancer Center. "In terms of NCI funding, there are 61 grants or projects already being funded. You could say that's not enough. But that's certainly not nothing. It's a pretty robust spectrum."

—"There is a lot of hesitation, including myself, in terms of the need for such an enormous structure at this stage," said board member Enrico Mihich, executive director for sponsored programs at Roswell Park Cancer Institute. "Nanotechnology—it means a lot, it means nothing. It's just an umbrella word," Mihich said. "Many aspects of nanotechnology are

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important and promising. I wonder whether it wouldn't be wiser to dissect these various aspects and discuss them with greater specificity in the light of bringing it into the area of oncology. What could be done with [the NCI proposal] that could not be done without it, or with less of it?"

—"I came to this meeting enthusiastic about nanotechnology and I'm still enthusiastic," said board member Richard Schilsky, associate dean for clinical research in the University of Chicago, Biological Sciences Division. "It's not that much money in the grand scheme of things. But, is this the most efficient way of getting results? I'm not convinced that a coordinating center is necessary. It's not clear what it would do. I do think training is important, but it's an awful lot of money up front."

"NCI Alliance for Nanotechnology in Cancer"

The proposal, called "NCI Alliance for Nanotechnology in Cancer," was developed over the past year-and-a-half, Institute officials said. According to the proposal, "NCI staff have solicited input from a broad cross-section of the cancer research and clinical oncology communities."

The Institute proposed funding three to five "Centers of Nanotechnology Excellence" to conduct research to develop applications of nanotechnology to cancer diagnostics, therapeutics, and prevention.

The program would include a coordinating center to collect data developed by the centers. Training components of the program would include career development and education grants.

"On the basis of discussions with a wide range of clinicians, cancer researchers, and technologists, it is clear that there are immense opportunities for using nanotechnology to solve mission-critical problems in cancer research," the proposal stated. "Nanotechnology offers the unprecedented and paradigm-changing opportunity to study and interact with normal and cancer cells in real time, at the molecular and cellular scales, and during the earliest stages of the cancer process."

NCI has supported "nanotechnology-based diagnostics and therapeutic strategies" for the past six years, the proposal said. The plan seeks to implement "a unified, comprehensive strategy designed to translate new technologies from the laboratory to the clinic."

The proposal states that "while select breakthroughs have demonstrated proof-of-concept that nanotechnology has great potential to overcome cancer, these advances have not been fully realized due to the lack of a cohesive vision and infrastructure necessary to support the myriad aspects of bench-to-bedside translation."

Funding for the nanotechnology project would include:

—Three to five U54 grants for Centers for Cancer Nanotechnology Excellence, $5.5 million in fiscal 2005 for planning, followed by $17.5 million in FY06, $19 million in FY07, $23 million in FY08, and $25.8 million in FY09, for a total of $90.8 million.

—One U01 grant for a Central Coordinating Center, with an annual budget of $1.5 million, for a total of $7.5 million.

—Multidisciplinary Career Development in Cancer Nanotechnology Research awards, consisting of 25 F33 Senior Fellows awards for $25 million; 15 K08 Mentored Clinical Scientist Development Awards and K25 Quantitative Awards for $15 million; six F32 Ruth L. Kirschstein National Research Service Awards for $450,000; and 50 to 75 T32 Institutional Grants of the NIH NRSAs for $3.75 million.

—An undetermined number of Cancer Nanotechnology Education R25 grants for a total of $6 million.

Last week, NCI released a "Request for Information" to encourage potential grantees or contractors to submit ideas about nanotechnology approaches to cancer diagnosis, treatment, and prevention. Responses are due Aug. 2. The RFI is available at http://grants1.nih.gov/grants/guide/notice-files/NOT-CA-04-022.html.

"Hard to Grasp the Entire Picture"

Horwitz and Curran, two of the board's three assigned reviewers of the proposal, were puzzled by the details of the plan.

"I would have liked to have read this before I came," Horwitz said at the BSA meeting. "I've never seen this before. I would like to have some references. I would like to read the literature. You said you had meetings over the last year and a half with experts in this area. I hope that some people on this board have been involved in those meetings. I haven't. We are asked to make very important decisions, in an area in which a lot of people don't know a tremendous amount about. The more you can help us understand, and we can read the literature, the better that we will be able to make intelligent decisions."

The proposal seems to overlap with a nanotechnology program included in the NIH

Roadmap for Medical Research, Curran said. "It's hard for me to grasp the entire picture of how this fits," he said.

The NIH nanotechnology program has the goal of developing clinical applications within 10 years, Curran said. "Your time frame is, of course, much shorter," he said to NCI officials. "You are looking at applications, from what I read, within a few years with this fairly aggressive kind of business plan that you are rolling out. I would have felt more comfortable with a broader-based cancer basic research program that had an R01 focus to complement the application side that you are developing here. I wonder if you are running the risk of duplicating some things that may be going on in industry right now, designed to make the same leap from discovery to application."

Curran said he was concerned about the role of industry in the program, "particularly given the current climate of how you manage that interface and the conflict of interest issues that will clearly arise as proprietary information is gained through these kind of partnerships." He said the proposal needed to describe more clearly how the relationship with industry would work.

"My greatest concern is that the extramural community is looking at a diminishing budget, and a potentially large set-aside to this new area will not be viewed as traditional investigator-initiated grant funded research," Curran said.

Board Chairman Frederick Appelbaum, the third reviewer, said he had a positive view of nanotechnology, but was skeptical about the project.

"Much can happen with nanotechnology if we understand the basis of the nanomaterials that can be built to create these building blocks," said Appelbaum, director of clinical research at the Fred Hutchinson Cancer Research Center. "I was able to have one of these [NCI-sponsored nanotechnology] symposia, and I was particular impressed in the area of early detection. I think in imaging, also, there may be great power, and in monitoring therapy. I'm less impressed with the ability to turn it into therapy, but even being able to monitor early therapy, I think there is great potential here.

"I agree, since we are a board that is asked to approve things, if there had been several members of the board involved in the development, the sociology of the board is that you trust the members to be your eyes and ears," he said. "That would have helped us a lot."

Appelbaum pointed out what he described as a flaw in the process of planning for centers of excellence.

First, the centers would receive $5.5 million to draw up initial plans. However, the NCI proposal contained no provision for evaluation following this initial stage.

"After the planning, you go right to $20 million to the centers," he said. "Does it matter what they plan? Is there any evaluation of the plan that would say, yes, we are ready to go to $20 million or we aren't? Is the science ready to invest $20 million a year at four or five centers? Maybe it will be or maybe it won't be. I don't know how that gets critically reviewed."

Appelbaum said he didn't understand the need for a coordinating center. "If you have such great science going on at the individual centers, is a coordinating center really going to tell you to reprioritize the materials you are going to use, and are you going to do that?" he said. "Can you just change your research focus on a dime? Does it really work that way? I don't know how effective that's going to be."

It's unclear how the experts trained under the educational grants will get funding once they are trained, Appelbaum said. "If we train 30 or 40 more people, will there be R01 money to absorb them? Is there going to be funding to absorb that large number of investigators in a three- or four-year period?

"Finally, I would have liked to have seen a much more detailed description of what is going on in industry, which is something I don't think we want to compete with," Appelbaum said. "If this is really the hot, new area, and if there are millions and millions and millions of dollars in start-up companies doing the same things that are being done here, that might put this at a lower priority. On the other hand, if there are specific reasons why industry isn't going into it, because they don't have the basic science, or they are very concerned about figuring out ways to test the safety of these materials, then we should hear from industry."

Appelbaum said looking to the future is part of NCI's role.

"I think it takes a lot of courage and future sight on the part of the director's office to look at the next technology and to say, 'Yep, we are going to put our foot down and we're going to go with the Director's Challenge,' as [former director] Rick [Klausner] did, for array analysis, and thank God he did it. I think it was a great thing."

Von Eschenbach: "Bold, Aggressive" Program

NCI Director Andrew von Eschenbach and Anna Barker, NCI deputy director for advanced technologies and strategic partnerships, spoke at length to try to convince the board to approve the program.

"I'm going to begin my comments by asking you to think big," von Eschenbach said. "This nanotechnology initiative is not occurring in a vacuum. I think many of you have been aware that there is a very significant commitment on the part of the Administration to the whole area of nanotechnology as an emerging technology that has significant scientific implications and also significant economic development implications. So there is a major commitment to the field of nanotechnology. For example, we have engaged with direct conversations and interactions with the Department of Commerce.

"We are not developing this in a vacuum, but we are doing it recognizing that there is a body of activity that is developing and emerging, primarily in materials sciences and for applications that are far outside the field of medicine," he said. "What we have the opportunity to do is to capitalize upon that and create a program with a cancer focus that will hopefully create a gravitational field that will enable that attraction and interaction, because the applications of nanotechnology are ultimately going to be what determines its value.

"If we can be at the forefront of the opportunity to create interest in the applications of nanotechnology to cancer, then we in fact have an opportunity to perhaps be at the forefront of what could be a significant advance," von Eschenbach said. "You're right. This is a risk. There is not already an enormous body of knowledge and data that absolutely guarantees that you've got a perfect investment. It is investment that is risky.

"In that regard, I've asked, and we've chosen, as I do in general, to give you full disclosure. We gave you a big number. $186 million is a big number.

"I personally feel, especially with the ramp-up, that the expenditures in the first few years will be more modest than they are in the last three years of the program," he said. "In an organization that has a total of a $4.8 billion budget, the outlay of approximately $36 million out of that on a yearly basis is not an inappropriate consideration for what could yield enormous returns, both to the point of view of how it can affect cancer research and that spreads across the entire spectrum of what the implications are in diagnostics, as well as in therapeutics, and in therapeutics, we are really talking about an area in which the distinction between what's therapeutic and what's preventive continues to blur, so it really spreads across prevention, detection, and therapeutic modulation.

"It also, I believe, creates an infrastructure in which, when you think about the training program component of this, builds intellectual capital as well. In this whole area of cancer research, biomedical research, I really think that attention to be able to create a core nucleus of people that can become expert in this area and that cross the chasm of the physical sciences and biologic applications of nanotechnology would position us in a way that we would have mentors and instructors three to five years from now that would significantly enhance and broaden the field.

"The gravitational force concept—and I really don't want to be taking too much of your precious time, but these are really important concepts—perhaps came home to me very distinctly on a visit to the cancer center at Vanderbilt, where I went over and visited their mass spec center, which is in the school of engineering, and talked to the director of that center," von Eschenbach said. "They have cancer center investigators working with the mass spec center, bring their cancer research projects to the center. The center's mission is to develop the whole technology of mass spec. But what he said was, this has been the greatest advantage to them, because the cancer researchers think they are getting the better part of the deal because they are using state-of-the-art equipment to answer their cancer questions. He said, 'We're getting the better part of the deal, because by our interaction with them, we are really understanding the questions that our technology is supposed to help answer. It's informing us as to how to really develop the technology.'

"Nanotechnology is going to go forward, whether the cancer enterprise is a part of it or not," von Eschenbach said. "It would be, I think, to our great advantage to create an infrastructure, an opportunity, and to make an investment that positions the cancer research community in a way that we could be at the forefront of not only informing the field as it is developing and looking for applications in the life sciences, but at the same time, positioning our community, basic researchers as well as clinical researchers, in a way that we really can be at the forefront of reaping the benefits of nanotechnology.

"Bold, aggressive, risky—you're right," von Eschenbach said. "Is it something that I believe is a significant opportunity, and have we put a lot of time, energy, and effort into testing that and evaluating that and attempting to bring to you something for which we think we have done a great deal of due diligence—yes, we have.

"I fully respect the fact that in addition to evaluating the scientific part, we have to do that in the context of realizing that resources are very precious, and that has also been a part of our consideration of this," he said. "That's why there are stringent—at least, we hope, we expect, and we anticipate that there will be—milestones and ongoing evaluations so that the investments are not going to be made in a blind or mindless kind of way.

"We also see this as having tremendous opportunities for developing and attracting resources so that—as someone asked the question, 'Is this going to go on forever?'—I've been around long enough to not be so naïve to realize that the hardest thing to do is to shut down programs," he said. "We are putting those kinds of things in place. It won't be a question of shutting down a program. I think it will be a prospect of finding other alternative revenue streams that will continue to nurture it, so that we can make our strategic investments, and perhaps by that time, five years or six years down the line, some other way."

Barker: "Transformational" Opportunity

Barker said the Nanotechnology Alliance could have a dramatic effect on cancer research.

"It's not often that one gets the opportunity to actually do something transformational, and I think that's what this is, and that's what we're struggling with," Barker said. "Frankly, we struggled with it. I think it is one of those transformational technologies.

"Why it's important and why it's going to be transformational is that at that [nano] level is where the forces of the cell come together that really drive the things we are thinking about, like signaling, for example," she said.

The program would provide NCI-funded cancer centers and Specialized Programs of Research Excellence a new opportunity, Barker said. "What we have attempted to do is to put together a program that would engage a broad sector of our community, using the strengths we have at our cancer centers, our SPOREs, but bringing in the opportunity to create these new clusters where we can actually develop this technology, train the next generation that we need, and really move this field forward," she said.

"Make no mistake, as Andy said, this [field] will go forward, with us or without us, whether we do it piecemeal or small—no pun intended—or whether we do it in a way that really engages the talent and the resources we have," Barker said. "If you think about it over five years, it approaches $40 million [a year], which, if you are in the technology business, trust me, really is not a lot of money, but if you are counting R01s, it is a lot."

Some of the funds for the program will come from the NCI Unconventional Innovations Program, started by former director Klausner, she said. "We believe that those funds ought to be reprogrammed to the broader community," Barker said. "What we are talking about a lot at the NCI about, when you say yes to something, you say no to something else. What we have been trying to look at is across all of our technology platforms, what could and should be reprogrammed here, and our Unconventional Innovations Program is one of those programs that would be reprogrammed into jumpstarting some of these activities."

Barker suggested the board delay its vote on the proposal until the next day, or a later meeting. "We want not to make a misjudgment at this point," she said. "There's no question that we are asking a lot of ourselves in terms of, do we have the courage? I have to tell you, it's been long in the planning, but in terms of transforming therapeutics and diagnostics, and potentially improving quality of life, there is probably not a better opportunity for us out there. We want to do the right thing. We've spent a lot of time on this and engaged a lot of the community. I don't want us to make a judgment that is rash or based on the dollar value versus what we are trying to accomplish."

Board Pulls In Different Directions

Following Barker's remarks, board member William Hait said he supported the proposal and considered it "a model" for translational research.

"Whether it's transformational or not, that's an open question, but I'd like to support this very strongly," said Hait, director of the Cancer Institute of New Jersey. "I've seen a team work on this in cancer pharmacology. It takes an unusual team of investigators to get together to do this.

"I think what we are struggling with is what we struggle in every think tank we go to on translational research, and that is team science and how to support

it through the NIH," Hait said. "The reason this isn't coming out as a series of R01 grants that we all are used to is that that won't work for this. You need a slightly different mechanism to allow these teams to function, to train, and to grow. For that reason, this very well presented, thoughtful RFA today, I would support it as a model of how the NCI can put its money where its mouth is in terms of translational research, whether it turns out to be transformational or not."

Board member Young suggested that NCI could fund nanotechnology research through regular funding mechanisms.

"We heard that NIH is focusing on this, industry is putting enormous resources into this," Young said. "It is a fundamentally cool thing. It's neat, and people are paying a lot of attention to it. That said, I'm not sure I understand the obstacles that you are conquering. What is the problem for which this is a solution? Is this simply an increased investment in this area because it's cool, or is this where we are trying to create novel structures to overcome obstacles to present science? If the latter is true, I missed it."

Barker said it's difficult for NCI to bring groups of scientists together. "In terms of how we bring these multidisciplinary teams together, we really don't have the platforms to do that, because we grew up in these small, very deep areas of reduction science," she said. "Nanotechnology is one of those integrating platforms that will allow us to bring in the physicists, the mathematicians, the oncologists, the pharmacologists, and do it in a way that potentially could allow us to translate science into the clinic."

Board member Margaret Spitz, chairman of epidemiology at M.D. Anderson Cancer Center, suggested delaying the training components of the program. "My feeling is that the educational component is premature and perhaps over-ambitious," she said. "The adjective I've heard associated with nanotechnology many times is 'emerging.' So if it's still an emerging technology, isn't it a bit premature to spend all these dollars on training programs for which I'm not sure we have sufficient trainers?"

Von Eschenbach said NCI would be willing to phase in the training grants later on or find alternative sources of funding, such as the National Science Foundation.

Hoda Anton-Culver, chief of epidemiology at University of California, Irvine, said she visited her institution's nanotechnology center and for that reason, she supported the proposal. "I think the way those centers ought to work is not to duplicate what can be done under any other technology," she said. "I really feel strongly that this is a very good thing to do, based on my first-hand meetings with a very good group of nanotechnologists."

Appelbaum asked members what action they wanted to take on the proposal. "We've had conversations going on all sides, from people who are truly enthusiastic, to those who are looking more for a compromise, to those who are somewhat skeptical, to those who suggested we table the issue without further discussions," he said.

Board member William Wood, chairman of surgery at Emory University School of Medicine, made a motion to approve the proposal, with the caveat that NCI shape the program "year by year" as needs change. "I don't see this as overcoming a barrier," he said. "I see this as an opportunity to accelerate a process, rather than just take logjams out of the way. The process is going to go forward anyway. This gives the opportunity to the NCI to both help it go forward faster and to channel it better."

Other board members indicated they would oppose approval without some conditions, including a slower phasing in of training. Von Eschenbach then offered to remove the two training components from consideration. However, program director Greg Downing, director of the NCI Office of Technology and Industrial Relations, objected to removing the training grants. He said a needs assessment would be done before starting the training program, and funds could be scaled back.

Young said NCI should include a process for ending the entire program. "When the three to five centers are established, they will like this mechanism," he said. "They will produce a lot of research, and people at NCI will like it. If you look at the history of big science, that's the mistake we make every time. At what point does the sun set?"

Barker and von Eschenbach said the nanotechnology plan includes specific milestones.

Paulette Gray, executive secretary of the board and acting director of the Division of Extramural Activities, suggested that NCI provide additional information to the board for discussion at a later meeting.

"I'm pretty proud of this board," said board member David Alberts, director of cancer prevention and control at Arizona Cancer Center. "The board is

doing its work. The solution is what Paulette suggested. Let's do this the way the board is comfortable working."

"We have been left out this year-and-a-half," Horwitz said. "We need to be clued in."

Curran made a motion to approve "in principle" the proposal, with the board to establish two subcommittees: one to analyze the proposal, and another to study nanotechnology.

Young said that plan was too complex. The board voted against the proposal.

Anton-Culver suggested that the board delay its vote on the nanotechnology alliance and establish just one subcommittee to study the science and the NCI proposal, and make recommendations to the full board in a conference call.

The board unanimously approved the motion.

In Brief:

Montgomery, 80, Developed Four FDA-Approved Drugs

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anti-cancer agents, anti-viral agents, anti-malarial agents, and insect chemosterilants. Four of his compounds were approved by the FDA for commercial use: fludarabine, dacarbazine (DTIC), lomustine (CCNU), and carmustine (BCNU). He is an inventor on two others that are currently in clinical trials: clofarabine, for which a new drug application has been filed with FDA by Ilex Oncology for pediatric leukemias; and 4'-Thio-ara-C, licensed to OSI Pharmaceutical Co. and in phase I trials.

Montgomery served on advisory panels to NIH and was a member of the Board of Scientific Consultants to the Sloan-Kettering Institute for Cancer Research from 1976-1985. During 1983-1985, he served on a steering committee of the World Health Organization. He received many awards, including the 1982 Cain Memorial Award from the American Association for Cancer Research, the 1986 Alfred Burger Award in Medicinal Chemistry and the 1995 Edward E. Smissman Bristol-Myers Squibb Award from the American Chemical Society.

He is survived by his wife Jean Kirkman Montgomery; two sons, John Montgomery Jr. and Kirkman Montgomery; two daughters, Elaine Montgomery Lees and Adrianne Montgomery Miller; and four grandchildren.

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REP. JOHN MURTHA (R-PA) announced funding for a research program in gynecologic cancer. Murtha obtained $4.2 million from the Department of Defense for the initiative, a collaboration among the University of Pittsburgh Cancer Institute, the Windber Research Institute, Walter Reed Army Medical Center, and Georgetown University to create a program dedicated to reducing the incidence, morbidity, and mortality of gynecologic cancers. "This program represents an important step in our effort to make significant advances in women's health—in this case, the prevention and treatment of gynecologic cancers and other debilitating diseases that have a tremendous impact on women," Murtha said.

The initiative will focus on characterizing the molecular alterations associated with benign and malignant gynecologic diseases and facilitate the development of novel early detection, prevention and treatment strategies for the management of gynecologic cancers such as ovarian, cervical and endometrial, as well as non-cancerous gynecologic diseases such as uterine fibroids and endometriosis.

The five aims of the program are to improve the ability to detect gynecologic diseases earlier, develop molecular profiling technologies, determine the influence of hormones on cancer risk, identify the molecular expression patterns associated with disease, and develop new therapies for gynecologic tumors.

The Telemedicine and Advanced Technology Research Center of the U.S. Army Reserve and Material Command will provide administrative and technical support for the initiative.

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UNIVERSITY OF SOUTH ALABAMA recently secured $24 million in additional funding to support a planned $40 million, 100,000 square foot building that will house the university's Cancer Research Institute. The funding came from private donations. The institute was founded in 2000 with state tobacco settlement funds, and currently has 37 employees. Its director, **Michael Boyd**, left NCI in 2002 after a 27-year career, most recently as director of the NCI Molecular Targets Development Program. He was chief of the Laboratory of Drug Discovery Research and Development from 1990-2001, and prior to that was director of the NCI Developmental Therapeutics Program from 1984-1990. Boyd said the center eventually plans to seek NCI cancer center designation. Further information about the institute is available at www.southalabama.edu/cri/.

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Business & Regulatory Report

Medicare Begins Demonstration Project Covering Oral And Self-Injected Drugs

The Centers for Medicare and Medicaid Services started a $500 million "demonstration project" covering oral and self-injected drugs.

The program, called Replacement Drug Demonstration Project, has the enrollment cap of 50,000 patients. Altogether, 13 cancer drugs will be reimbursed through the program which will run through Dec. 31, 2005.

Constrained by the overall spending cap and the limitations on enrollment, CMS focused the demonstration project on cancer, multiple sclerosis and rheumatoid arthritis.

Drugs and biologics selected for coverage must eliminated the

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Approvals & Applications:

Tarceva Accepted On FDA Pilot 1 Program For Faster Review, Approval Of NDAs

OSI Pharmaceuticals Inc. (Nasdaq: OSIP) of Melville, NY, said the New Drug Application for Tarceva (erlotinib HCl), has been accepted onto the FDA Pilot 1 Program for Continuous Marketing Applications.

The Pilot 1 Program is designed for products that have been designated Fast Track status and have demonstrated significant promise in clinical trials as a therapeutic advance over available therapy for the disease or condition.

As one of the Prescription Drug User Fee Act goals, the Pilot 1 Program is designed to expedite the Continuous Marketing Application (otherwise known as "Rolling NDAs") Concept.

Under the program, applicants with products meeting the requirements are eligible to submit a limited number of portions (or "Reviewable Units") of their NDA in advance of the complete application. The FDA has agreed to complete reviews of the individual Reviewable Units as they are submitted and to provide early feedback to the applicant. OSI had previously been granted Fast Track status for the advanced NSCLC indication in September 2002 and submitted the non-clinical and CMC sections of the NDA under the standard "rolling submission" provision on Jan. 20, 2004.

With the Pilot 1 Program designation the FDA is committed to initiating the review of these sections on a six month review timeline as of the notification of Pilot 1 status. OSI also announced that it has filed the BR.21 study report with the FDA which follows on from the filing of

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CMS Begins Project To Cover Oral, Self-Injected Drugs

(Continued from page 1)

concurrent need for a currently covered drug or biological for a currently covered indication. Covered therapies must have FDA approval for the indication and must be at least of equal efficacy to the covered drug it replaces. Use of the therapies must represent an advantage in terms of access and convenience, compared to the currently covered drugs, and only drugs commonly provided incident to a physician service will be covered.

"Covering drugs that you can administer yourself improves access to high-quality care," CMS Administrator Mark McClellan said in a statement. "In some cases, by avoiding the need for doctor visits and intravenous injections, costs and medical complications may be reduced and access and ease of treatment will increase. And many beneficiaries will get literally tens of thousands of dollars worth of help in purchasing these critical medicines right away, ahead of the Medicare drug benefit in 2006."

The following cancer drugs have been included:

—Targretin (bexarotene) for cutaneous T-cell lymphoma.

—Iressa (gefitinib) for non-small cell lung cancer.

—Hexalen (altretamine) for epithelial ovarian cancer.

—Gleevec(imatinib mesylate) for chronic myelogenous leukemia and gastrointestinal stromal tumor.

—Temodar (temozolomide) for anaplastic astrocytoma.

—Thalomid (thalidomide) for multiple myeloma.

—Hormonal therapies for stage 2-4 breast cancer: Arimidex (anastrozole), Aromasin (exemestane), Femara (letrozole), Nolvadex (tamoxifen), Fareston (toremifene).

Altogether, 40 percent of funds allotted to the project would be used to pay for cancer drugs.

Next year, the cost sharing formula will include a $250 deductible, and 25 percent cost-sharing for the first $2,000 in drug costs. After that threshold, the program would pay the entire cost of drugs until the bill reaches $3,600. After that, the benficiary's contribution will amount to 5 percent of cost of the covered drug or a fixied copayment of $5 for branded drugs.

Additional details are available from CMS at: www.cms.hhs.gov/researchers/demos/drugcoveragedemo.asp

To qualify for the program, a beneficiary must have Part A and Part B Medicare, and must rely on the program as the primary health insurance. If the number of applicants exceeds the number of slots, CMS will randomly select participants.

Application forms for the program will be available from the CMS Web site starting July 6, and coverage for enrolled patients would begin on Oct. 18.

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Approvals & Applications:

OSI Expects To Complete Tarceva Filing This Summer

(Continued from page 1)

the first clinical section on May 12, 2004. OSI expects to complete its NDA filing for Tarceva over the summer and, assuming a priority review the action date will be six months from the completion of the NDA submission.

* * *

Amgen Inc. (Nasdaq: AMGN) said it submitted a Biologics License Application with FDA for palifermin, an investigational compound for oral mucositis.

The potential therapeutic indication is to reduce the incidence, duration and severity of oral mucositis in patients with hematologic malignancies undergoing

high-dose chemotherapy, with or without irradiation, followed by a bone marrow transplant.

The BLA was submitted under the Fast Track designation program. "Palifermin is a first-in-class, innovative biologic that protects the epithelium of the mouth and gastrointestinal tract from damage caused by anti-cancer therapy," said Beth Seidenberg, chief medical officer and senior vice president of global development at Amgen.

The company said the BLA filing contains data from the phase III pivotal study of palifermin which demonstrated that patients with hematologic malignancies undergoing high-dose chemotherapy, with or without irradiation, and bone marrow transplant support who received palifermin suffered less ulcerative oral mucositis (grades 2-4) compared to those receiving placebo (15.7 days vs. 8.4 days). In addition, palifermin helped protect patients from the most severe form of oral mucositis (grade 4) with 20 percent of palifermin-treated patients experiencing this painful and debilitating side effect, compared to 62 percent of placebo-treated patients.

Serious adverse events occurred at the same rate in patients who received palifermin or placebo (21 percent), the company said. The most frequently reported serious adverse events in both groups were fever, gastrointestinal and respiratory related.

Most adverse events were attributable to the underlying malignancy, cytotoxic chemotherapy, or total body irradiation and occurred at similar rates in patients who received palifermin or placebo. Other adverse events were consistent with the pharmacologic action of palifermin on skin and oral epithelium and included rash, pruritus, erythema, edema, mouth/tongue thickness or discoloration, and taste disorders. These events were mild to moderate in severity and were reversible, the company said.

* * *

ImClone Systems Inc. (Nasdaq: IMCL) of New York said the European Commission has approved Erbitux (cetuximab), an IgG1 monoclonal antibody, in combination with irinotecan for the treatment of patients with metastatic, EGFR-expressing colorectal cancer after failure of irinotecan-including cytotoxic therapy:

Erbitux will be available in all 25 member states of the newly expanded European Union as well as Iceland and Norway, according to local legal regulations for supply.

The approval was granted to **Merck KGaA** of Darmstadt, Germany, based on its European clinical trial that included more than 300 patients with metastatic colorectal cancer. Merck licensed Erbitux from ImClone in 1998, and holds the rights to develop the agent outside of the U.S. and Canada, and has the co-exclusive right to develop it in Japan.

In another development, ImClone said FDA approved the company's Chemistry, Manufacturing and Controls supplemental Biologics License Application (sBLA) for licensure of its manufacturing facility (referred to as BB36).

BB36 is a 30,000 liter capacity, single-product manufacturing facility dedicated to the production of Erbitux. From the beginning of 2002 through the end of 2003, the Company produced approximately 200 kilograms of bulk product which is equivalent to 400,000 doses of Erbitux. At maximum capacity, BB36 is expected to produce 250 kilograms of bulk product per year.

* * *

ILEX Oncology Inc. (Nasdaq:ILXO) of San Antonio said FDA has been granted priority review of its NDA for clofarabine for refractory or relapsed acute leukemia in children.

Clofarabine was granted orphan drug designation for adult and pediatric acute lymphoblastic leukemia and acute myeloid leukemia, the company said. Clofarabine is a next generation of the drug class purine nucleoside analogs which all inhibit DNA production for cancer cell growth, the company said.

Bioenvision Inc. (AMEX:BIV) sub-licensed ILEX the right to develop and market clofarabine for cancer indications in the U.S. and Canada. Bioenvision is entitled to milestone payments tied to the development of the compound and is entitled to royalties on North American sales, the company said. Bioenvision originally obtained clofarabine development and commercialization rights under patents held by Southern Research Institute.

Clinical Trials:

Angstrom Begins Phase II For Ovarian Cancer Product

Angstrom Pharmaceuticals Inc. of San Diego said it has begun a phase II trial of its proprietary product, A6, for the prevention of clinical relapse in ovarian cancer.

The 48-60 patient study is designed to assess the safety and efficacy of the product in asymptomatic women in clinical remission who have an elevated CA-125 tumor marker level following successful first

line treatment, the company said.

A6 targets the urokinase plasminogen activator system, which has been implicated in cancer progression, the company said. Preclinical studies have shown the product inhibits cell migration and cell invasion and blocks the supply of blood to tumors. In phase 1 studies, daily injections of A6 were shown to be safe and well tolerated.

Angstrom Pharmaceuticals Inc. is a privately held company.

* * *

BBCI of Kansas City, Mo, said it is providing clinical trial management services to **BioCryst Pharmaceuticals Inc**. for its phase IIa trial with forodesine hydrochloride, a purine nucleoside phosphorylase inhibitor T-cell cancers.

Forodesine hydrochloride, a small-molecule drug which causes biochemical changes that result in blocking of the DNA synthesis machinery of the T-cell, received orphan drug designation from FDA for T-cell non-Hodgkin's lymphoma, the company said.

The multi-center, global, open-label study would determine the efficacy of long-term dosing with forodesine hydrochloride, the company said. The study will be divided into two parts, phase IIa and IIb. The phase IIa study will evaluate response rate and duration of response in 20 patients with refractory T-cell leukemia who have failed or relapsed previous treatment.

* * *

ILEX Oncology Inc. (Nasdaq:ILXO) of San Antonio said it has begun a multi-center phase II study of ILX-651 for hormone-refractory prostate cancer where the disease has progressed after first-line treatment with Taxotere (docetaxel).

ILX-651 is a tubulin-interactive agent that has shown preliminary activity in a range of solid tumors, the company said. Two additional phase II studies with ILX-651 are ongoing in metastatic melanoma and non-small cell lung cancer.

The non-randomized, open label 40 patient study will take place at 10 to 12 clinical sites, the company said. Intravenous treatment with ILX-651 will daily for 5 consecutive days every 21 days. Treatment with ILX-651 would continue for up to one year.

Results of a phase I study showed that ILX-651 to be biologically active and well-tolerated in advanced refractory solid tumors, the company said. Preliminary safety data from the phase II metastatic melanoma trial showed the drug to be safe, tolerable and convenient as administered in that trial.

ILX-651 is a next-generation synthetic pentapeptide analog of the natural substance dolastatin with a unique mechanism of action that potentially differs from that of microtubule-stabilizers (taxanes and epothilones) and tubulin inhibitors (vinca alkaloids and other dolastatins), the company said. The drug has been chemically modified to provide improved pharmacological properties and is orally bioavailable with an enhanced therapeutic window over earlier-generation dolastatins.

* * *

ImClone Systems Inc. (NASDAQ:IMCL) New York, N.Y., and **Merck KGaA** of Darmstadt, Germany (Frankfurt Stock Exchange: MRK) said the international, randomized phase III trial of IMC-BEC2 cancer vaccine did not meet its primary endpoint of survival for small cell lung carcinoma.

IMC-BEC2 is an investigational anti-idiotypic monoclonal antibody that mimics GD3, a ganglioside expressed on the cell membrane of most small cell lung cancer tumors, the companies said. The study was conducted in collaboration with the cooperative group European Organisation for Research and Treatment of Cancer.

The trial was designed to assess the survival benefit of vaccination with IMC-BEC2 and the immune stimulant BCG over a two-year period, the companies said. Patients were randomized into either the treatment arm, receiving IMC-BEC2/BCG vaccination, or into the observation arm.

* * *

Merix Bioscience of Durham, NC, said it has begun a phase I/II study of an RNA-loaded autologous dendritic cell vaccine newly diagnosed metastatic renal cell cancer.

The trial is taking place at five sites in the U.S.and Canada, the company said.

The RNA-loaded dendritic cell vaccine is composed of dendritic cells taken from a patient and infused with amplified RNA from his or her tumor. The personalized vaccine primes the immune system to recognize and fight the cancer utilizing tumor-specific targets, said Fred Miesowicz, acting head of clinical development at Merix. Another study objective includes demonstrating the safety and commercial feasibility of processing dendritic cells at a central manufacturing facility with delivery of the vaccine to multiple clinical sites, he said.

* * *

OSI Pharmaceuticals Inc. (Nasdaq:OSIP) of Melville, N.Y., and **Genentech Inc.** (NYSE:DNA)

said they have entered into two agreements detailing their respective promotion, marketing and manufacturing responsibilities for Tarceva (erlotinib HCl) in relapsed non-small cell lung cancer, once it is approved for distribution in the U.S.

A phase III trial of the investigational drug was successfully completed and an NDA rolling submission to FDA is ongoing, the company said.

As stated in the original 2001 agreement to co-develop and commercialize the drug in the U.S., Genentech will continue its responsibility for the marketing, launch and promotion of the drug, the companies said. OSI will assist with by providing at least 25 percent of the combined U.S. sales force. The companies will continue to share responsibility for the ongoing development post-launch. OSI is responsible for obtaining the current approval by the FDA and is working to complete the NDA for the treatment during the summer of 2004.

The second agreement covers the OSI responsibilities in the commercial manufacturing and supply of Tarceva in the U.S. market, the companies said.

* * *

Point Therapeutics Inc. (NASDAQ:POTP) of Boston said it has begun a phase II trial of talabostat (PT-100) for advanced metastatic melanoma.

The study would evaluate the anti-tumor and hematopoietic activity of the agent in combination with cisplatin for advanced metastatic melanoma, the company said.

The single-arm, two-stage 54 patient study has a primary clinical endpoint of overall tumor response, the company said. At mid-point, tumor response rates will be compared to historical response rates of current therapies to determine whether the trial should be continued. Other secondary study endpoints include complete response rate, duration of tumor response, time to disease progression, survival and incidence of severe neutropenia and anemia.

* * *

Therion Biologics Corp. of Cambridge, Mass., announced the initiation of a phase III trial of PANVAC-VF, a vaccine for the treatment of metastatic pancreatic cancer in patients who have not responded to treatment with gemcitabine.

The trial will enroll 250 patients at 50 to 60 participating treatment centers across the US. The study's primary endpoint will be overall survival, compared with palliative chemotherapy or best supportive care.

The study is being conducted under the guidance of a Special Protocol Assessment provided by FDA. The SPA indicates that if the trial successfully meets its primary endpoint, the data will provide the basis for an efficacy claim in a marketing application to the FDA.

The trial design is based on data presented this month at the Annual Meeting of the American Society of Clinical Oncology. The company said data from two separate phase I studies of Therion's investigational vaccines demonstrated a median overall survival of 7.9 months and at least 5.3 months, respectively, in patients with advanced pancreatic cancer, compared to an anticipated median overall survival of approximately three months, based on historical controls.

PANVAC-VF is designed to stimulate the immune system to target and destroy cancer cells expressing two proteins, carcinoembryonic antigen (CEA) and mucin-1 (MUC-1), found on over 90 percent of pancreatic tumor cells. The vaccine also incorporates TRICOM, Therion's proprietary triad of costimulatory molecules (B7.1, ICAM-1 and LFA-3), designed to enhance and sustain a targeted immune response against tumor cells.

The multicenter, randomized, controlled trial will enroll 250 patients with advanced pancreatic cancer in whom gemcitabine is ineffective. Patients will be randomized 1:1 to receive either PANVAC-VF or control treatment. Patients in the treatment arm will receive an initial dose of PANVAC-VF plus GM-CSF to initiate an anti-cancer immune response, followed by a series of "booster" vaccinations to sustain the response. Control treatment will consist of either best supportive care or palliative chemotherapy (capcitabine, irinotecan or 5-fluorouracil). Secondary study endpoints include safety, quality of life parameters, change in serum tumor antigen levels, response rate and disease stabilization.

* * *

Wilex AG of Munich, Germany, said has begun enrollment for phase III study of it antibody, Rencarex(WX-G250), for in renal cell carcinoma.

The multi-center, global, randomized study has been designated ARISER (Adjuvant Rencarex Immunotherapy trial to Study Efficacy in non-metastasized Renal Cell Carcinoma) and is evaluating the efficacy of the antibody versus placebo as an adjuvant therapy for clear cell RCC.

Patients who are disease-free following the

surgical removal of the kidney but who have a high risk of developing metastatic RCC will be enrolled in the study, the company said. The study is designed to detect a significant difference between the two treatment arms with respect to disease-free survival; patients will be followed-up long-term to determine overall survival statistics.

The 612 patient trial will take place in over 50 sites in Europe and the US, the company said. The treatment arm will be treated for six months with a once-weekly infusion of Rencarex. The other arm will be monitored with regular CT scans.

Wilex said it has recently been granted IND approval for the phase III trial by FDA.

Rencarex (WX-G250) is a IgG1 monoclonal antibody that binds to a cell surface antigen, the MN-antigen (also called G250-antigen or CA IX), which is found on 95 percent of clear Renal Cell Carcinoma cells but not on normal tissue, the company said.

* * *

Xanthus Life Sciences of Cambridge, Mass., said it has begun a phase I trial for Symadex (formerly C-1311) for advanced solid tumors.

Symadex is a next-generation anti-cancer agent designed to have similar or improved efficacy compared to the chemotherapeutic, Novantrone (mitoxantrone), with reduced side effects, including cardio- and hemato- toxicities, the company said. In the trial, the treatment will be evaluated in a once weekly infusion cohort and will subsequently be evaluated in additional dosing regimens.

Deals & Collaborations:

Pfizer To Buy Irinotecan If Sanofi Buys Aventis

Sanofi-Synthelabo said it has signed an agreement with Pfizer Inc regarding the divestment of Aventis' interests in Campto (irinotecan) in response to requests made by the antitrust authorities.

Subject to the consent of the US Federal Trade Commission and the success of Sanofi-Synthelabo's offer for Aventis, Pfizer will take over key clinical studies for Campto that are currently conducted by Aventis.

The $620 million deal also includes patents and other assets pertaining to territories where Pfizer currently markets irinotecan. Pfizer will further, subject to certain conditions including clearance by European competition authority, acquire all other Aventis assets related to Campto.

Aventis markets Campto, which was first launched in 1995 under a license from Yakult Honsha Company Ltd., primarily in Europe, Asia and Africa. In 2003, Aventis' sales of Campto reached euro 264 million.

* * *

Active Biotech AB of Lund, Sweden, said it has signed an agreement with **Strathmann Biotec AG** of Hamburg, Germany, to develop and manufacture the Active Biotech cancer product TTS (tumor targeted Superantigens) CD3 for non-small cell lung cancer.

The agreement with Strathmann Biotec, based on co-development of the product, will secure a cost efficient long-term development and manufacturing plan, including the possibility for future large volume commercial production, the company said.

Strathmann Biotec will take an active part in the project and share a part of the financial risk, the company said. In return, SB is entitled to a limited royalty on the AB income from future milestones and sales.

TTS CD3 is a biotechnology product which is produced using recombinant E. coli based expression system, the company said.

The production of the product will be transferred from the present manufacturer (Biovitrum) to Strathmann Biotec, the company said.

A phase I dose-escalation study of TTS CD3 is in progress for non-small cell lung cancer at the Fox Chase Cancer Center and at the Radiumhospitalet in Oslo, Norway, the company said. A first generation of the product, TTS CD2, has concluded phase IIa trials in renal and pancreatic cancer.

* * *

Agilent Technologies Inc. of Palo Alto, Calif., said it is collaborating with the **Translational Genomics Research Institute** on comparative genomic hybridization, an application of oligonucleotide microarray technology that identifies and locates genetic alterations that contribute to cancer.

CGH is used to identify regions of chromosomes that have been lost or multiplied in cancer cells, allowing the tumors to escape normal growth controls, the company said.

Agilent Labs., the central research facility of Agilent Technologies, is collaborating with TGen to validate and further develop commercial microarray-based CGH solutions based on the Agilent custom in situ manufacturing process, in which DNA

oligonucleotides are synthesized base by base directly on a glass slide.

"The ability to closely analyze and view gene expression and high-resolution CGH data side by side could yield unprecedented insights into the nature of various cancers," said Jeffrey Trent, president and scientific director of TGen. "In addition to shedding light on how tumors arise, the data could provide the foundation for diagnostic and prognostic tools, and help identify the most promising targets for drug development."

The joint effort builds on a six-year, ongoing collaboration on gene-expression profiling between Trent and the scientists at Agilent, the company said. Trent was scientific director of the National Human Genome Research Institute and served as chief of its Cancer Genetics Branch before leading the establishment of TGen in 2002.

* * *

Brigham and Women's Hospital of Boston said it has granted **ZymeQuest Inc.** of Beverly, Mass., an option to license the worldwide rights to a method of treating and chilling blood platelets.

The technology, which could prolong the shelf-life of platelets by a week or more, was conducted by the BWH Department of Hematology with scientific support and assistance from ZymeQuest. Under a joint invention agreement, BWH and ZymeQuest share the proprietary rights to the technology.

"Platelet modification is based on the proprietary use of a naturally occurring sugar compound (UDP-galactose) and state-of-the-art methods and processes to modify platelets such that they may be stored under refrigeration," said Thomas. Stossel, lead investigator of the technology, co-director and senior physician of the hematology division at BWH, American Cancer Society Professor of Medicine at Harvard Medical School and a member of the ZymeQuest board of directors. "The license grants ZymeQuest the rights to product development and commercialization of the carbohydrate modified platelet technology, which produces a modified platelet product offering several advantages."

"Because of refrigerated storage, this technology is expected to provide a much safer transfusion product that could decrease the cost and complexity of platelet inventory management, improve the efficacy of platelet transfusions, simplify the process of collection and storage, and reduce platelet outdating losses significantly, said Stossel. "With the aging population in the U.S. and the number of young donors decreasing, this technology could revolutionize the operation of blood centers."

The demand for platelets has increased by an annual rate of 15 to 17 percent during the past five years, according to data published by the American Association of Blood Banks and the National Blood Data Resource Center. Despite the increase in demand, 20 percent of the platelet supply outdated and was discarded in each of those years. In 2001, the cost of outdating in the U.S. is thought to have exceeded $155 million.

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Kalypsys Inc. of San Diego and **NIH** entered into a $30 million agreement in which NIH will use the Kalypsys proprietary technologies in its Chemical Genomics Center.

The center will produce chemical tools used to understand the function of the genes that comprise the human genome.

The Kalypsys platform is comprised of off-line and on-line capabilities, including workstations, hit-picking, essential consumables, compound libraries, compound acquisition and screening services, and an ultra-high throughput screening system capable of screening in excess of one million compounds per day in a variety of biochemical and cellular assays, the company said.

The NIH Chemical Genomics Center is the first in a consortium of chemical genomics screening centers being established by the Molecular Libraries and Imaging Initiative with leadership from the National Institute of Mental Health. Up to 10 pilot centers will be funded at academic institutions and other locations across the country in fiscal year 2005. To support the network, NIH will establish a repository to acquire, maintain and distribute a collection of up to 1 million chemical compounds, said NIH.

* * *

Matritech Inc. (AMEX:MZT) of Newton, Mass., and **Wampole Labs**., a wholly owned subsidiary of Inverness Medical Innovations Inc., said they have entered into an agreement for the distribution of the Matritech NMP22 Test Kit.

Under the agreement, Wampole will receive exclusive rights to distribute the NMP22 ELISA Test Kit to hospitals and clinical reference laboratories in the U.S., the companies said. Matritech will continue to sell the NMP22 BladderChek Test directly to urologists.

The NMP22 Test Kit is a microplate enzyme immunoassay that detects elevated levels of NMP22 protein, the company said. The protein is often found at elevated levels in the urine of patients with bladder cancer, even at early stages of the disease. The test is a quantitative tool that identifies hidden or rapidly recurring disease.

* * *

Phylonix of Cambridge, Mass., said it has received a $993,463, phase II small business innovation grant from **NCI** to develop zebrafish apoptosis assays for drug screening.

"Apoptotic cells in live, transparent zebrafish can be visualized by acridine orange staining without complicated processing," said Chuenlei Parng, principal investigator at Phylonix. "We are also developing a quantitative, vital dye assay for high throughput screening using an automated liquid handling workstation and a microplate reader."

The company is developing a family of drug screening assays using the small vertebrate zebrafish. The animal model will serve as an intermediate step between cell-based evaluation and animal testing for drug evaluation, the company said.

* * *

iCAD Inc. (Nasdaq:ICAD) of Nashua, N.H., said FDA has approved the release of the iCAD Second Look 200 system for early detection of breast cancer. The system makes CAD accessible to smaller Breast Care Centers, the company said.

The system analyzes up to 15 cases per day, is fully automated, fits on a counter top and is priced below $70,000. Version 6.0 detection software offers up to 94 percent sensitivity to all breast cancers.

In a related development, Scan-Optics Inc. (OTC BB:SOCR) of Manchester, Conn., said its manufacturing services division has received a contract from **iCAD Inc.** to manufacture the iCAD Second Look 400 Series Computer Aided Detection of Breast Cancer Product Line, which received FDA approval.

The contract provides for product shipments this quarter and volume shipments will begin in the third quarter, the company said.

In another development, **Confirma Inc**.of Kirkland, Wash., said it has formed a strategic alliance with **iCAD Inc.** to market an enhanced version of the iCAD Second Look system.

Confirma will provide CADstream, the standard in CAD for breast MRI, to iCAD for integration with the Second Look 500 CAD system for mammography, the company said. iCAD will market and distribute the new version of Second Look with the integrated CADstream system. Confirma will continue to directly market and distribute CADstream.

CADstream technology automates data analysis, improves image management and corrects for patient movement, the company said.

* * *

Target Software of Allentown, Pa., said it has entered into a licensing and services agreement with the **OSI Pharmaceuticals Inc**. Oncology Business to implement and operate the Target SFA sales effectiveness suite.

The suite will become the OSI central sales information management solution and the Target Software Support Center will provide training, hosting, help desk, data management and other SFA operational services for OSI, the company said.

The OSI national sales force is being deployed on Target Mobile sales software, the company said. OSI oncology sales specialists will use account- based selling features of Target Mobile, including account profiling, affiliation management, route planning, event management and sales data presentation.

Target BackOffice will become part of the OSI Pharmaceutical central sales data warehouse and CRM solution, the company said.

Patents:

Firms Share Patent For GPC's Cell-Cycle Inhibitor of Cdks

GPC Biotech of Martinsried/Munich, Germany, and **U.S. Research Facilities** of Waltham/Boston, Mass. and Princeton, N.J., said the U.S. Patent and Trademark Office has issued GPC Biotech a patent with claims covering RGB-286199, its cell cycle inhibitor.

Claims also include pharmaceutical compositions, as well as methods of treating diseases, including cancer, the company said. The patent, whose term will expire in late 2022, is pending in Europe, Japan and Canada

RGB-286199 is an inhibitor of cyclin-dependent kinases or Cdks, associated with the development of cancer, the company said. Anticancer activity of RGB-286199 has been demonstrated in animal models of ovarian, prostate, and colon cancer.

GPC Biotech said it would complete pre-clinical development of the drug candidate in the first half of 2005 and advancing into clinical trials thereafter.

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