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Accelerated Approval Will No Longer Block Competitors, FDA Commissioner Says

CHICAGO—Cancer drugs approved based on "surrogate endpoints" under the FDA accelerated approval mechanism will no longer block competitors from entering the market, FDA officials said last week.

Under the agency's new interpretation of the accelerated approval regulations, only agents that receive full approval after demonstrating benefit to patients would block competitors from entering the market.

In recent years, some sponsors who received accelerated approvals seemed to be in no rush to complete post-approval studies and convert their agents to full approval. Now, the agency's action is likely to lend

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In Brief:

Tempero, Johnson Take ASCO Offices; Society Recognizes Community Oncologists

MARGARET TEMPERO, a medical oncologist widely respected for her work in gastrointestinal cancers, began a one-year term as president of the American Society of Clinical Oncology on June 2, during the society's annual meeting in Chicago. **David Johnson**, a lung cancer specialist, became president-elect, and six new board members began three-year terms. **Paul Bunn Jr.**, who completed his term as ASCO president, remains a member of Board of Directors as the immediate past president. Tempero is deputy director of the comprehensive cancer center at University of California, San Francisco, where she also serves as chief of the Division of Medical Oncology. Johnson will succeed Tempero as ASCO president in 2004. He is the Cornelius Abernathy Craig professor in medical and surgical oncology and deputy director of the Vanderbilt-Ingram Cancer Center at Vanderbilt University Medical School. **Larry Norton** was elected chairman of the Board of Directors of the ASCO Foundation. Norton is head of the Solid Tumor Division at Memorial Sloan-Kettering Cancer Center. He succeeds **Alan Lichter**. New board members are: **David Gandara, Patricia Ganz, Michael Perry, Le Helman, Joseph DiBenedetto Jr.,** and **Jose Baselga**. New members of the Nominating Committee are **Kathleen Pritchard** and **Sonja Eva Singletary**. . . . **COMMUNITY ONCOLOGY** practices were recognized by ASCO for participating in clinical trials: **Neil Abramson**, of Baptist Cancer Institute; **Frederick Schnell**, Central Georgia Hematology Oncology Assoiates; **Ferdinand Addo**, Medcenter One Health System; **Alan Lyss**, Midwest Hematology Oncology

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FDA Action May Lend Urgency To Finishing Phase IV Studies

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urgency to such studies, triggering competition to the finish line of full approval.

"Other drugs would also be able to get accelerated approval status for that indication until one of these therapies demonstrates through phase IV study commitments a clinical benefit in patients," said FDA Commissioner Mark McClellan at the annual meeting of the American Society of Clinical Oncology.

McClellan announced the change during a joint presentation May 31 with NCI Director Andrew von Eschenbach, where heads of the two agencies announced their plans for collaboration in development and approval of cancer agents.

"This is something that we think NCI's recent help in funding more phase IV studies reinforces," McClellan said. "We are going to have stronger incentives than ever for getting phase IV studies completed."

As NCI and FDA pledged to work together, the differences in their positions seemed striking.

FDA is a practical "show-me" agency that seeks to apply scientific standards as uniformly as possible. NCI is an agency with a mission. Guided by a plan by Director von Eschenbach to "eradicate death and suffering from cancer" by 2015, the agency regards FDA as a gatekeeper.

Von Eschenbach said he first came to McClellan's office to discuss ideas for a collaboration the morning after the FDA Commissioner was confirmed by the Senate.

"I kind of barged into his office, and immediately expressed my excitement for the opportunities that we have now available to us, based on the progress that has been made in biomedical research, and how important it was for us to translate that progress into interventions," von Eschenbach said at ASCO.

Speaking with precision, and frequently consulting his notes, McClellan laid out a plan of collaboration built on his agency's reliance on NCI as a science agency.

"We set the world's gold standard for care of patients with cancer and other diseases," McClellan said. "We are going to remain committed to approving only safe and effective drugs."

McClellan said he is concerned about the drop in the number of drug approvals, the rising cost of drug development, and the falling success rate in clinical trials.

"A lot of experts are attributing these trends to the changing nature of medical technology development, with an increasing reliance on biotechnology and emerging sciences like genomics and proteomics that are primarily still in the early stages of development, leading to a lot of research investment, but not new products yet," he said.

"I think we can compress what may otherwise be a very long process of moving these treatments down the pipeline through better support for translational research."

McClellan's plans included:

—Playing a role in NCI's review of the clinical trials process. "We think NCI support for developing methods that can improve our understanding about the relationship between potential biomarkers that can be observed relatively early in the clinical development process and clinically important endpoints can help our regulatory activities a lot," McClellan said.

FDA and ASCO recently cosponsored a series of workshops to assess the evidence on surrogate endpoints "with the goal of developing clear guidance about efficient pathways to regulatory approval for major solid cancers."

—Leveraging NCI and FDA programs building a "more inclusive bioinformatics platform that can capture and integrate data from clinical research

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World Wide Web: http://www.cancerletter.com

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

Editorial: 202-362-1809 Fax: 202-318-4030
PO Box 9905, Washington DC 20016
E-mail: news@cancerletter.com

Customer Service: 800-513-7042
PO Box 40724, Nashville TN 37204-0724
E-mail: info@cancerletter.com

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across all of the sectors of the development process," McClellan said.

—Increase FDA representation on NCI advisory boards and NCI representation at FDA boards, and form joint training and joint appointment programs in oncology. "It would enable us to improve the science base and the understanding of the latest scientific knowledge at both agencies," McClellan said.

—Explore the implications of pharmacogenomics. "That work is still really in its infancy, and there is a ton of information out there that we don't have any clear idea of what it means for regulatory decision implication which are based on implications for clinical outcomes in patients," McClellan said. "Our hope is that by pooling our efforts in developing this applied knowledge base, we can eventually permit better-targeted, less costly and more efficient clinical testing in patients."

Von Eschenbach said the two agencies would collaborate to "accelerate the ability to take the fruits of our research and be certain that that's translated into lives that no longer have to suffer and will no longer die because of the disease like cancer." Specifically:

—NCI will involve FDA in an impending review of the clinical trials system.

"Over this next year, NCI will embark upon a very intensive effort to look at our whole clinical trials infrastructure, and to look at ways that we can adapt and modify our clinical trials effort to really be responsive to the tremendous opportunities that are now before us, with the fruits of genomics and proteomics," von Eschenbach said.

"We may need to design new biomathematics and biostatistical models," he said. We may need to look at our ability and will look at our ability to integrate multiple interventions that are based on mechanistic interruptions, recognizing that those interventions singly may appear to be ineffective, but in combination would in fact be quite effective at dealing with progression of disease."

—The regulatory agency will be asked to help in validation of surrogate endpoints.

"Looking at that from the point of view of embarking upon applications of new technologies in molecular profiling, looking at the opportunity of expanding on the surrogate endpoints that FDA currently uses by scientifically evaluating biomarkers for those surrogate endpoints, so that they can appropriately and rationally be incorporated into our process," von Eschenbach said.

—FDA will be involved in the Institute's drive to apply surrogate endpoints to chemoprevention.

"Within cancer prevention [there is] a whole emerging role of chemoprevention, and the work in the science that needs to be done with regard to our ability to integrate chemopreventive strategies into our clinical arena," von Eschenbach said. "Work needs to be done in appropriately validating those interventions and having the science to underpin their approval, and then to be able to monitor them as chronic administration over a period of time."

—FDA would play a role in dietary interventions, von Eschenbach said.

"NCI will be placing a great deal of emphasis on the issue that we describe as 'energy balance,' or the interaction between diet and physical activity," von Eschenbach said.

"With regard to diet, there are extraordinary needs and opportunities in that arena. Diet is an issue that for us—even from HHS—has become a major strategic initiative, because of the epidemic of obesity in this country and for the implications it has with regard to Type II diabetes, and cardiac disease, as well as cancer," he said.

"As we look at diet, and as we look at the need to further develop the science of understanding dietary factors and micronutrients, we also need to be working collaboratively and cooperatively with FDA in terms of how to validate the impact in a way that they can make recommendations with regard to dietary guidelines."

ASCO Policy: "Nothing Less Than A Smoke-Free World"

CHICAGO—Calling for the eventual elimination of smoking, the American Society of Clinical Oncology assembled world leaders in tobacco control to urge governments and health organizations to renew attention to the "global health crisis caused by tobacco products."

ASCO President Paul Bunn, a lung cancer expert and director of the University of Colorado Cancer Center, unveiled the society's new tobacco policy statement, which calls for the formation of an independent commission to develop a blueprint for worldwide reduction in, and eventual elimination of tobacco use.

"Our new policy defines our ultimate goal: nothing less than a smoke-free world," Bunn said in an address at the ASCO annual meeting on June 2.

"As a lung cancer specialist, I'm sick and tired of watching cancer patients suffer and die from tobacco-induced cancers to fill the greed of tobacco companies," Bunn said to sustained applause from the audience of cancer specialists. "As an American, I'm horrified that we are exporting this greed and death-inducing substance around the world."

Joining ASCO in support of the tobacco control statement were Sir Richard Peto, of the Clinical Trials Service Unit at Oxford University; Nigel Gray, of the European Institute of Oncology; Dileep Gal, of the California Department of Health Services; Richard Hurt, director of the Nicotine Dependence Center at Mayo Clinic; John Seffrin, CEO of the American Cancer Society and president of the International Union Against Cancer; and Rev. Jesse Brown, president of the Coalition for World No Tobacco Day.

ASCO's policy statement calls for immediate steps, including:

—Increasing efforts to discourage tobacco use, particularly among the young.

—Raising federal excise taxes by at least $2 per pack and encouraging states to consider tobacco taxes as a first resort in revenue enhancement.

—Ensuring that tobacco settlement funds be devoted only to health-related projects, including medical treatment, biomedical research, and tobacco prevention.

—Requiring disclosure of all ingredients in tobacco products.

—Comprehensively reforming third-party payment for tobacco cessation efforts.

—Further restricting secondhand smoke in any places where the public may congregate.

—Supporting research into tobacco addiction, toxicities, and prevention strategies.

—Enhancing global tobacco control including a halt to U.S. government promotion of tobacco products.

The full text of the ASCO statement is available at www.asco.org.

Bunn: ASCO "Strong, Diverse, Respected, And Growing"

CHICAGO—Completing his one-year term as the president of the American Society of Clinical Oncology, Paul Bunn said the society is "strong, diverse, respected, and growing."

ASCO has 20,000 members, a budget of $45 million, and 145 full-time staff working on public relations, public policy, journals, news and services, guidelines, and meetings, said Bunn, director of the University of Colorado Cancer Center.

Excerpts of Bunn's remarks follow:

ASCO is strong, diverse, respected, and growing. Membership continues to grow at an impressive rate, adding about 450 members each quarter, to a total that now exceeds 20,000. The largest numbers are still American, but ASCO is becoming increasingly international, with about half of the new members coming from outside the U.S. The majority of members are still medical oncologists, but the number of non-medical oncologists is also increasing.

ASCO now looks more like a true cancer center, with representation from all specialties and support professionals.

The annual meeting attracted a record number of abstracts this year [3,200 submissions]. These numbers are a real tribute to the progress generated from clinical and translational studies. Meeting attendance has now leveled at about 26,000 attendees. The JCO continues to increase its numbers of subscribers, articles published, and index ratings.

I'm especially pleased that we were able to fund 49 young investigator and career development awards this year, a record number of training awards, particularly since the number of applications more than doubled in just the past year.

The details of the ASCO budget, income, and expenses were reviewed during the business meeting, and the financial status of the society is sound. Last year, the total operating budget exceeded $45 million, and the long record of operating in the black continued. This year, the projected revenues and income both exceed those of last year. ASCO now has over 145 staff at its Alexandria, Va., headquarters. Most importantly, the ASCO Foundation, under Larry Norton's leadership, has increased both the amount and the diversity of the funds raised. These funds from the foundation are critical for our training grants, our patient and public awareness efforts, our Web services, and many other initiatives.

Now, I would like to focus your attention on ASCO's mission of improving cancer care and prevention. The cancer patient lies at the heart of this mission. I want to highlight ASCO's accomplishments by first focusing on areas of particular importance to me. These topics, honoring people with cancer, and tobacco control, are the themes of this year's meeting.

The central nature of the cancer patient was recognized at the first ASCO meeting right here in

Chicago 39 years ago, when Dr. Goudsmit noted, "The single most important factor behind our first meeting is our common concern for the patient with cancer." The overriding conviction that more can and should be done for the majority of cancer patients.

In support of this ideal, I'm proud we have dedicated the theme of this meeting to "Commitment, Care and Compassion," to honor people with cancer. In addition, our award-winning patient Web site, www.peoplelivingwithcancer.org, has received a record number of visits. I anticipate this Web site will only increase in size and value in future years.

I'm also proud of our increasing partnerships with patient advocate organizations. These have allowed us to fund an increasing number and diversity of grants, and have helped us move forward many of our quality cancer care initiatives. For example, the support of the Komen Foundation has helped our National Initiative on Cancer Care Quality, begun by Dr. [Joseph] Bailes. The first results from this landmark study were presented at this meeting.

We completed our prevention survey in partnership with the Cancer Research and Prevention Foundation. Our partnerships with the NCCS and Friends of Cancer Research have helped with our legislative advocacy efforts.

Since we have decided this is the year to honor patients with cancer, I want to extend my own personal appreciation to Ellen Stovall [CEO of the National Coalition for Cancer Survivorship] and the many other patient advocates who help us in our work.

Cancer prevention has always been a major element of the ASCO mission. To meet the increasing importance of prevention, we created a new prevention standing committee. One of the first actions of this committee was to undertake a survey of current prevention practices of U.S. physicians, and patient attitudes, done in collaboration with the Cancer Research and Prevention Foundation. The first results of this survey were presented at this meeting.

Tobacco Control

Of course, one of the most important prevention issues that of tobacco control. A task force chaired by David Pfisters [of Memorial Sloan-Kettering] drafted bold revisions to our tobacco policy that the Board of Directors approved in May.

As a lung cancer specialist, I'm sick and tired of watching cancer patients suffer and die from tobacco-induced cancers to fill the greed of tobacco companies. As an American, I'm horrified that we are exporting this greed and death-inducing substance around the world.

Our new policy defines our ultimate goal: nothing less than a smoke-free world. This policy calls for the formation of an independent commission to develop a blueprint by which immediate reduction in tobacco use and eventual elimination become a reality. The commission's plan must be comprehensive, and it must include agricultural, regulatory, trade issues, promotion, and First Amendment rights issues. It must consider all of the world-wide economic and social issues.

This policy calls for increased tobacco taxes, expanded prevention programs, limitation on promotion, trade restrictions and other measures. I trust that ASCO's policy will inspire our governments to bold and definitive solutions to eliminate this true weapon of mass destruction.

International Issues

Because half of all of our new members are from non-U.S. sites, our strategic plan calls for us to meet all member needs. Thus, I chose to focus on international issues. To understand national and regional society operations, I and other ASCO leaders met with the major societies at our annual meeting, and undertook a trip around the world last June to meet with various organizations.

We have created positions for representatives of these organizations on our International Affairs Committee. This committee has worked with the expanded International Affairs Department to accomplish many of the strategies defined on the slide.

At this meeting, your passage of the Bylaws has created a second international seat on the Board of Directors. We have increased the number of international travel awards to the annual meeting to 16. We have provided each with a mentor and have made arrangements for each of these young oncologists from developing countries to visit one of our comprehensive cancer centers.

Medical oncology is a well-established specialty within the U.S. and parts of Europe, but there are no established training programs in many parts of the world. We are working with our colleagues in ESMO, who have a great record in training criteria, to develop model guidelines for training certification in medical oncology for these developing countries.

The ASCO board has approved funding for an international multidisciplinary management course.

Our joint symposium with ASH, ESMO, and FECS will be expanded this fall to a symposium in Argentina with FLASKA. We jointly sponsored meetings with the International Association for the Study of Lung Cancer this year, and are providing support for expansion of the fellows course in clinical trials to Australia with the Medical Oncology Group of Australia.

U.S. Reimbursement Issues

As ASCO is guided by an unwavering commitment to our patients and their welfare, we are proud of our joint efforts to respond to those in the U.S. Congress and the federal government who would challenge and potentially undermine quality cancer care by imposing reimbursement cuts that would, indeed, threaten access to outpatient care as we know it. Recent events highlight the perilous nature of the current situation.

ASCO has long recognized the distorted nature of the current system, distorting payments for both drugs and services. We cannot allow the Congress or Medicare to slash reimbursement for cancer drugs, without a simultaneous correction for the serious underpayment for chemotherapy administration service and other essential outpatient services. ASCO has worked diligently with government officials to provide financial data on these outpatient services through our sponsored surveys.

We have worked with the Cancer Leadership Council and advocacy groups to gather support for the Cancer Quality Care Preservation Act, or HR 1622, recently introduced by Reps. Norwood and Capps. This bill proposes that chemotherapy drugs are reimbursed at their actual sales price, or ASP, plus 20 percent, rather than the current system of 95 percent of AWP. Further, the bill would establish payment codes for chemotherapy administration and for other outpatient services that reflect the true actual costs of providing these critical services.

We are delighted that every important oncology organization, ranging from proprietor groups to patient advocates have rallied around this legislation. I'm particularly pleased that so many of you came to Washington on May 20 to meet with your own congressmen and women. However, much remains to be done, and it's up to you, our members, to follow through.

Oral chemotherapies are increasing in number and effectiveness. We must continue to work with our patient partners in the Congress to support the Access to Cancer Therapies Act providing Medicare coverage for these new oral anticancer drugs.

New Meetings, Publications Planned

The increased size and diversity of ASCO has created the need to provide educational and research venues beyond this annual meeting and beyond the JCO. This is especially critical as each disease-oriented group desires to have their own meetings and their own journals. The splintering off of multiple disease-oriented groups is a real threat to ASCO if we do not meet our member needs.

To address these needs, we have experimented with several new meetings and meeting types. These include a second educational meeting on molecular oncology for the practicing oncologist, held in Chicago last fall. We held the first non-annual meeting that was abstract-driven on molecular therapeutics for the academic oncologist in November. We held the first joint workshop with a disease-oriented group, the International Association for Lung Cancer. The first workshop was held in Spain. The proceedings will be published as a companion to the JCO and sent to all ASCO members. Another joint meeting with the IASLC will held in Brazil next year. We held the first interactive education program via satellite with the Clinical Oncology Society of Australia.

Next year, we have planned for a major new disease-oriented meeting on gastrointestinal cancers, and this will be jointly sponsored with ASTRO, SSO, and the AGA. The meeting will take place in San Francisco in January. There will be both abstract-driven and educational sessions.

Another new meeting is the Best of ASCO meeting, sponsored jointly with regional affiliates. While the annual meeting has more than 25,000 attendees, many member physicians cannot attend, but want to understand these abstracts that might change their practice. This year, the Program Committee identified abstracts that would most influence standard practice. These were developed into a Best of ASCO curriculum and are available to state and regional affiliates to use in planning Best of ASCO meetings. The Northeast Regional Affiliates will sponsor the first of these meetings, in Boston, in September. If this format is successful, this will be expanded to other parts of the country next year. It is anticipated that these meetings will have far greater balance than many post-ASCO meetings sponsored by industry.

Although the JCO is the premier clinical

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oncology journal, our member surveys have indicated that multidisciplinary disease-oriented monographs and reviews, plus topics in molecular oncology, were unmet needs of high priority. To address this need, the board and Publications Committee have developed plans to expand the JCO, beginning in January 2005, to include molecular oncology and clinical reviews. We are also adding supplements to the JCO, and first of those just appeared on ovarian cancer.

We will be publishing the ASCO Educational Book from this meeting in a citable form so the abstracts can be cited in the literature.

Clinical Research

Clinical research has always been a cornerstone of our mission. However, recent events and well-publicized scandals have brought increasing public scrutiny to clinical trials.

To maintain the integrity of and public trust in the system, we have developed a conflict-of-interest policy. This policy calls for disclosure of all financial arrangements, and sets prohibitions for general conduct of clinical trials for principle investigators and others who might inappropriately influence clinical trial results.

A standing Ethics Committee was established to provide guidance on these and other ASCO issues.

The board also adopted a policy statement on the oversight of clinical trials that calls for establishing central IRBs to oversee national trials sponsored by both industry and government. ASCO has begun working with the NCI to determine how to best implement this policy.

The Clinical Trials Task Force recognized that a large fraction of patients are accrued to trials through community practice, and a small minority of practices accrue the vast majority of these patients. To reward these important practices, Community Practice Clinical Investigator Award were established and presented at this meeting for the first time.

It was also recommended that ASCO develop a best-practices curriculum and workshop for community practices to emulate those of the award-winners. This curriculum and workshop will be developed and taught by the successful practices, including both physician and research staff of these practices.

ASCO has recognized the lack of clinical trial expertise in our own staff, and a new full-time position was created. The Clinical Trials Task Force also recognized many of the most important clinical trials have difficulty accruing patients, because of the complex nature of the trial. To facilitate accrual to such difficult trials, we instituted a new educational symposium at this meeting on high-priority trials.

ASCO has begun working with the NCI to develop a national clinical trials informatics system.

Finally, recognizing that rapid and rational FDA approval is the goal of new drug discovery, we worked with the FDA to establish endpoints for drug approvals. This was a partnership with ASCO and the FDA, and the endpoints will be done on a disease-by-disease basis.

This effort of ASCO and the FDA includes advocates, industry, oncologists, and statisticians to consider endpoints for lung cancer trials. Next year, we will expand this to other diseases, including breast, prostate, and colorectal cancers.

ASCO Staff A "Delight"

This year has been an amazingly educational one for me, and it has been made extremely enjoyable by ASCO's outstanding volunteers and staff. It has been a delight to work with ASCO's full-time staff. They are amazingly efficient and unbelievably dedicated. There is no way to pay sufficient credit to ASCO's senior directors. I guess I began to understand their diligence when my cell phone went off on a Sunday morning when I was out snowmobiling with Dr. Balch. This was the morning the New York Times article on the "cancer concession" broke. By the time Dr. Balch and I returned from snowmobiling, ASCO staff had already prepared our draft response, and email messages which were sent to all members.

From public relations, to public policy, to journals, news and services, guidelines, meetings, ASCO staff is the best, and ASCO is respected because of their work….

ASCO has an unbelievable Board of Directors. They are willing to debate issues, and think and act strategically. They will never say no and they are always available for emergency executive phone calls, of which we had three in the past month. I will miss you all.

How does ASCO accomplish so much when there are more than 20,000 members? Believe it or not, ASCO has more than 700 volunteers. There are 23 standing committees, with 600 volunteers and five task forces, with another 100 volunteers. That does not even count the 46 affiliated regional and state oncology societies. They have performed a great service for you this year.

In Brief:

NCI's Kalt To Advise Gates

(Continued from page 1)

Consultants Inc.; **Pat Whitworth**, Nashville Breast Cancer Center; **P. Gregory Rausch**, Oncology Care Consultants; **Stanley Vogel**, Cotton O'Neil Clinic, Stormont Vail Health Care; **William Demas**, Summa Health Systems; and **Nick Spirtos**, Women's Cancer Center at Community Hospital Los Gatos. . . . **MARVIN KALT**, director of the NCI Division of Extramural Activities, transferred to the NIH Office of the Director, where his title is senior advisor for special partnership projects. Later this month, he plans to move to Seattle, where he will work on loan from NIH to the Global Health Program of the Bill and Melinda Gates Foundation to help establish the foundation's grant programs. Kalt is a 23-year veteran of NIH. He worked at the National Institute on Aging before moving to NCI 13 years ago. **Paulette Gray**, DEA deputy director, was named acting director of the division. . . . **M.D. ANDERSON** Cancer Center received a five-year $500,000 unrestricted cancer research grant from Bristol-Myers Squibb Co. The grant will support translational research, with a focus on biologic approaches to cancer prevention and treatment, molecular changes that can be used for early diagnosis, and development of targeted treatment strategies. **Waun Ki Hong** will supervise and serve as principal investigator. Hong is Samsung Distinguished University Chair in Cancer Medicine, professor and chairman, Department of Thoracic/Head and Neck Medical Oncology, and head, Division of Cancer Medicine. . . . **JAMES MOHLER** was named chairman of the Department of Urology at Roswell Park Cancer Institute. He was associate professor of surgery, pathology, and laboratory medicine, Lineberger Cancer Center, and director of the Prostate Cancer Research Program, University of North Carolina, Chapel Hill. Roswell Park also made appointments to its Dept. of Cancer Genetics: **Nicoletta Sacchi**, associate professor of molecular genetics, University of Milan, Italy; **Andrei Bakin**, assistant research professor, Dept. of Medicine, Vanderbilt University School of Medicine; **Irwin Gelman**, director of virology research and research associate professor, Mount Sinai School of Medicine; and **Keshav Singh**, assistant professor of oncology and environmental health, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins.

NCCN National Comprehensive Cancer Network

Regional Guidelines Symposia

NCCN member institutions throughout the country host regional NCCN guidelines symposia. These seminars provide small groups of community oncologists with the opportunity to hear talks given by NCCN guidelines panel members. Participants gain in-depth understanding of a specific NCCN clinical practice guideline, including the issues considered when developing it and in managing the target disease. Participants discuss the guideline as it relates to their professional practice and provide feedback from the community perspective.

For more information about these programs including agendas, speakers, educational credits, dates, locations, or sponsorship opportunities, visit www.nccn.org or call 866-788-NCCN (6226).

Program Dates

2003 NCCN Non-Hodgkin's Lymphoma Guidelines Symposia

- June 20 – New York City
  Host: Memorial Sloan-Kettering Cancer Center
- June 24 – Denver
  Host: Huntsman Cancer Institute at the University of Utah
- September 9 – Chicago
  Host: Robert H. Lurie Comprehensive Cancer Center of Northwestern University
- September 23 – Boston
  Host: Dana-Farber Cancer Institute

2003 NCCN Multiple Myeloma Guidelines Symposium

September 18 – Houston
Host: University of Texas M. D. Anderson Cancer Center

2003 NCCN Breast Cancer Guidelines Symposia

- October 30 – Atlanta
  Co-hosts: Duke Comprehensive Cancer Center

  University of Alabama at Birmingham Comprehensive Cancer Center
- November 5 – San Francisco
  Co-hosts: Stanford Hospital & Clinics

  UCSF Comprehensive Cancer Center

These dates are subject to change.

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Business & Regulatory Report

Product Approvals & Applications:

Velcade Given Accelerated Approval For Third-Line Treatment Of Myeloma

FDA gave accelerated approval to Velcade (bortezomib) injection, a third-line treatment for multiple myeloma. Velcade, distributed and marketed by Millennium Pharmaceuticals, Inc., of Cambridge, Mass., is the first in a new class of anticancer agents known as proteasome inhibitors.

FDA reviewed the application for this drug in less than four months. The agency evaluated the safety and efficacy of Velcade based on

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Oncology Management:

ASCO Tech Assessment Group Maintains Recommendation On Use Of Arimidex

The Technology Assessment Working Group of the **American Society of Clinical Oncology** voted unanimously to support and maintain its recommendation issued last year regarding Arimidex (anastrozole) tablets for postmenopausal women with hormone receptor-positive early breast cancer.

The 47-month follow-up data from the Arimidex early breast cancer trial (ATAC—Arimidex, Tamoxifen, Alone or in combination) provide "a greater level of assurance, in terms of both toxicity and efficacy, for physicians and their patients who are considering the use of anastrazole in the adjuvant setting," the working group said.

The data continue to support the previous recommendation that the tablets be considered for postmenopausal women with hormone receptor-positive early breast cancer who may be at high risk for some of the side effects associated with tamoxifen, such as blood clots and stroke.

Arimidex is the only hormonal drug other than tamoxifen that has been approved for use in the adjuvant setting.

The effectiveness of the therapy is based on an analysis of recurrence-free survival from the ongoing Arimidex early breast cancer trial in patients taking Arimidex following surgery with or without chemotherapy and radiation for a median of 2 1/2 years, and thus allows only a preliminary comparison with tamoxifen, the working group said.

The 47-month follow-up data showed no substantial difference in either efficacy or toxicity from the 33-moth data, and there are too few events for a mature survival analysis between the treatment and tamoxifen

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FDA Approves Velcade For Multiple Myeloma

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a study of 202 patients who had received at least two prior therapies and demonstrated disease progression on their most recent therapy. Altogether, out of 188 patients evaluated for response, 28 percent showed a response to Velcade. The response lasted a median time of one year. Another trial in 54 patients with relapsed multiple myeloma showed similar responses.

"As a result of close collaboration among the company, NCI, and FDA in the development and review of the drug, FDA was able to make this novel therapy available sooner to help many thousands of patients suffering from multiple myeloma," said FDA Commissioner Mark McClellan. "The approval of Velcade illustrates FDA's commitment to providing patients with access to safe and effective drugs as quickly as possible."

As of yet there are no controlled trials of Velcade demonstrating clinical benefit, such as improvement in survival. To address this issue, Velcade's developer will perform additional studies after approval. These will include the completion of an on-going study and an additional study comparing Velcade to standard therapy.

"The drug shows a significant effect on patients with multiple myeloma that have not responded to other treatments – a response that is likely to result in significant clinical benefit," said McClellan. "As with other treatments approved under our accelerated approval process, further studies are necessary for clarifying Velcade's clinical benefits."

The most commonly reported adverse events reported in clinical trials include nausea, fatigue, diarrhea, constipation, headache, decreased appetite, decreased platelets and red cells in the blood, fever, vomiting, and peripheral neuropathy.

* * *

ImClone Systems Inc. (Nasdaq: IMCLE) and **Bristol-Myers Squibb Co.** (NYSE: BMY) said the companies met with FDA to discuss clinical trial data including the Merck KGaA-sponsored 007 phase II trial of the investigational drug Erbitux (cetuximab) for metastatic colorectal cancer as well as data from completed ImClone Systems-sponsored clinical studies.

Based on the outcome of this meeting, ImClone Systems intends to submit a Biologics License Application in the second half of 2003, for approval of Erbitux for the treatment of metastatic colorectal cancer, the company said.

The 007 study was a randomized, two-arm, multi-center phase II trial evaluating Erbitux monotherapy and the combination of Erbitux and irinotecan in 329 patients with irinotecan-refractory, EGFR-expressing colorectal cancer.

In the combination therapy arm, study findings showed a 22.9 percent response rate, 4.1 month median time to progression and 55.5 percent overall rate of disease control. Results of the cetuximab monotherapy treatment group showed a 10.8 percent response rate, 1.5 month median time to progression and 32.4 percent overall rate of disease control. Median survival time was 8.6 months for patients treated with the combination therapy and 6.9 months in patients treated with cetuximab monotherapy. The differences in response rate and median time to progression were statistically significant. The most common severe toxicities reported in the study were diarrhea (21.2 percent in the combination treatment arm vs. 1.7 percent in the monotherapy group) and acne-like rash (9.4 percent vs. 5.2 percent). Severe allergic reactions were reported in four patients.

The 007 study was presented June 1, at the annual meeting of the American Society of Clinical Oncology in Chicago.

In ImClone and Merck entered into a license agreement that gave Merck the right to develop

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cetuximab outside the U.S. and Canada and the co-exclusive right to develop cetuximab in Japan.

* * *

Pall Corp. (NYSE: PLL) of East Hills, N.Y., said FDA has granted marketing clearance for its Leukotrap WB Filtration System.

The system incorporates the patented sterile air venting elimination technology, an automated blood recovery and air removal device that recovers of red blood cells and plasma, the company said.

After whole blood is collected, air is traditionally forced out of the blood bag by manually squeezing the bag before the blood undergoes additional processing prior to transfusion, the company said. Technicians can squeeze as many as 60 bags per hour, one bag every minute. The SAVE system automatically removes the air, eliminating this manipulation step.

The Leukotrap WB Filtration System with SAVE will be available to blood centers soon, the company said.

Oncology Management:

ASCO Maintains Advice On Use Of Arimidex

(Continued from page 1)

groups, the group said.

"Arimidex offers women a treatment option other than tamoxifen," said Aman Buzdar, principal U.S. investigator, of M.D. Anderson Cancer Center. "Because the treatment continues to show improvement over tamoxifen, more and more physicians may discuss it as an option with their early breast cancer patients."

* * *

National Comprehensive Cancer Network of Bridgewater, N.J., issued Cancer and Treatment-Related Anemia Practice Guidelines for physicians for management of cancer and treatment-related anemia.

The guidelines cite the connection between hemoglobin levels and symptom management; highlight the importance of early intervention for treatment-related anemia in patients with erythropoietic agents, such as Procrit (Epoetin alfa); and provide treatment algorithms for the use of anti-anemia erythropoietic agents, the network said.

Chemotherapy-related anemia, which affects 71 percent of cancer patients, is a manageable and treatable side effect, but is often is unrecognized and left untreated, the network said.

NCCN Anemia Panel members made the following recommendations for treating chemotherapy-related anemia: treatment of anemia should be considered when hemoglobin levels are less than 11 g/dL. Treatment recommendations include the use of Epoetin alfa 40,000 units once-weekly or 10,000 units three times per week and darbepoetin alfa 2.25 mcg/kg weekly. Physicians should evaluate hemoglobin levels at week four of treatment with Epoetin alfa compared with week six with darbepoetin alfa. The guidelines recommend that non-responders receive a 20,000 unit increase in Epoetin alfa to 60,000 units QW or 10,000 unit increase TIW to 20,000 units TIW. Non-responders with darbepoetin alfa should increase their dose up to 4.5 mcg/kg QW.

NCCN Cancer and Treatment-Related Anemia Practice Guidelines are available at www.nccn.org/physician-gls/f-guidelines.html under the Guidelines for Supportive Care section or by visiting www.Cancer.com and looking for the link to NCCN in the Side Effects section.

Clinical Trials:

ARIAD Begins Phase I Trials Of Agent For Solid Tumors

ARIAD Pharmaceuticals Inc. (Nasdaq: ARIA) of Cambridge, Mass., said it has begun enrollment in two phase I studies of AP23573, a cancer product candidate for advanced solid tumors.

The AP23573 class of cancer drugs inhibits the protein mTOR and shrinks tumors by metabolic arrest through inhibition of nutrient uptake to tumor cells, as well as inhibition of growth factor stimulation, the company said.

Using different dosing regimens, the studies of 35 to 50 patients are designed to evaluate the safety and tolerability, pharmacokinetics and pharmacodynamics of the product candidate, the company said.

Gene markers will explore the relationship between the anti-tumor activity and genetic mutations of tumors, the company said.

"Expediting the clinical development of AP23573 is our top R&D priority this year, and we anticipate initiating phase II development of AP23573 in targeted cancer indications as early as possible next year," said Harvey Berger, chairman and CEO of ARIAD.

* * *

Eximias Pharmaceutical Corp. of Berwyn, Penn., said the second meeting of the independent data safety monitoring board resulted in a unanimous recommendation to continue the phase III evaluation of thymitaq for hepatocellular carcinoma.

The agent exerts its anticancer activity through direct inhibition of thymidylate synthase and is the only cytotoxic with clinical data showing a survival advantage in liver cancer, the company said.

The DSMB met in December 2002 and at that time supported the continuation of the trial based upon an evaluation of 141 patients, the company said. The DSMB met for the second time in May 2003 to review the safety data of 220 patients randomized by the end of 2002.

Mark Buyse, chairman of the DSMB, congratulated the company on the quality of the data presented and for the way the trial is being conducted, said Jose Garcia-Vargas, vice president of clinical development at Eximias.

The phase III ETHECC trial is underway at 70 sites in the US, Canada, Europe and South Africa, the company said.

* * *

Ortho Biotech Products LLP of Bridgewater, N.J., announced the results from a phase II study evaluating the combination of Doxil (doxorubicin HCI liposome injection), vincristine and a reduced-dose of dexamethasone, known as DVd, for multiple myeloma.

The 33-paitent study, conducted at the Cleveland Clinic Myeloma Research Program of the Taussig Cancer Center, investigated the safety, tolerability and efficacy of the DVd combination regimen, the company said. At least six cycles of the DVd regimen were administered, during which, patients were given intravenous Doxil (40 mg/m2) and vincristine (2 mg) on the first day, and oral or intravenous dexamethasone (40 mg/day) for four days. The treatment regimen was repeated every four weeks.

Eighty-eight percent (29 patients) responded to treatment with the DVd regimen, the company said. Of these patients, four (12 percent) achieved a complete response, defined as complete disappearance of myeloma protein from the serum and urine by immune fixation, a bone marrow biopsy demonstrating less than 3 percent plasma cells, the absence of monoclonal plasma cells by immune staining of the bone marrow on two occasions at least four weeks apart, and no evidence of progressive disease by any other parameters. Eighteen patients (55 percent) had a major response, defined as a 50 percent or greater decrease of myeloma protein from the serum and urine, while seven patients (21 percent) had a minor response, defined as a decrease in bone pain, an improvement of performance status by one grade, and a reduction in serum myeloma protein of 25 percent or greater. The median time to progression in the study was 23.1 months with two-year and three-year progression-free survival rates of 42 percent and 23 percent, respectively, the company said. The patient survival rate at three years was 67 percent.

The most common grade 3 or 4 toxicity reported in the study was palmar-plantar erythrodysesthesia—a skin reaction that usually occurs on the palms of the hands and the soles of the feet. This occurred in five of the first nine patients enrolled; however, with improved patient education and prevention, only two of the remaining 24 patients enrolled experienced toxicity of this magnitude.

Other grade 3 and 4 toxicities reported were mucositis (inflammation and ulceration of the lining of the mouth, throat or gastrointestinal tract); neutropenia (low white blood cell count), anemia (low red blood cell count), and thrombocytopenia (low platelet count). No growth factors were necessary and no patients were hospitalized for neutropenic fevers or intravenous antibiotics. Six patients required packed red blood cell transfusions and one patient required a platelet transfusion. Only one patient experienced cardiotoxicity.

Dose reductions were required in six patients and treatment was delayed due to adverse events in one patient. The incidence of grade 1 and 2 adverse events was not reported by the authors in the publication. No patients discontinued treatment due to adverse events.

* * *

Progenics Pharmaceuticals Inc. (NASDAQ: PGNX) of Tarrytown, N.Y., said it has begun a phase II trial of the investigational drug, methylnaltrexone, for post-operative ileus, a paralysis of the gastrointestinal tract.

"Virtually all patients who undergo abdominal, laproscopic, or prolonged surgical procedures experience bowel dysfunction," said Robert Israel, senior vice president of medical affairs. "If MNTX can reverse this form of bowel paralysis, it has the potential for broad clinical utility in post-operative patients. We believe that physicians may be able to use MNTX to decrease the duration and severity of

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post-operative ileus and to accelerate recovery and discharge."

To evaluate the tolerability and clinical activity of MNTX in POI, a multi-center, randomized, double-blind study is being conducted in 60 individuals who have undergone colectomies, the company said.

Shortly after surgery, patients will receive either placebo or a 0.30 mg/kg dose of intravenous MNTX, the company said. Study medication will then be administered every six hours until the recovery of bowel function. The endpoints of the study include restoration of bowel function and discharge eligibility.

Prior to the phase II trial in post-operative ileus, the company said it had conducted a phase I trial of MNTX dosing in normal volunteers. Twelve individuals received intravenously administered MNTX (0.30 mg/kg) every six hours for three days. Repeated dosing with MNTX produced a 20 percent (p(less than)0.05) decrease in mean oral-cecal transit time, a measure of the rate at which ingested food moves through the gastrointestinal tract. The findings suggest that endogenous opioids may play a role in the modulation of gastrointestinal motility. There were no serious side effects reported in the study, the company said.

Deals & Collaborations:

Adherex Enters Agreement With NCI On Drug Candidates

Adherex Technologies Inc. (TSX: AHX) of Ottawa said it has entered into a screening agreement with NCI to evaluate the anticancer effects and vascular targeting capabilities of compounds from the Adherex library of proprietary cadherin antagonists.

Under the agreement, NCI will assess the drug candidates in vitro as well as in preclinical animal models, the company said. The classes of agents include peptide cadherin antagonist compounds for N-cadherin, E-cadherin, desmogleins, VE-cadherin and OB-cadherin, as well as the Adherex third generation small molecule, non-peptide cadherin antagonists.

"The agreement brings the enormous capabilities of NCI to the evaluation of the agents and will accelerate the timeframe for the potential development of these compounds into clinically useful agents," said William Peters, vice chairman of the board and CEO of Adherex Technologies Inc. "NCI has extraordinary scientific capabilities and resources that will be used to evaluate the relative effectiveness and to help us understand the mechanisms of action of our drugs. We would not have had the resources to conduct these studies on our own."

* * *

A.I. Software Inc. (OTCBB:ASOW) of Vancouver, B.C., said it has reached an agreement with the **Weitzman Institute of Science and Technion—Israel Institute of Technology** to acquire the exclusive rights of stem cell expansion technology.

The patented technology, in its developmental stages, could enable cord blood transplants in adults, the company said.

The technology expands stem cells from umbilical cord blood without differentiation, allowing better results in cord blood transplants in adults, the company said.

Under the agreement, A.I. will have the licensing rights to a stromal cell bioreactor—a process and protein that assists in restoring the bone marrow in adults with leukemia, lymphomas, autoimmune disease and other blood-related disorders, the company said.

A.I. said it is acquiring the rights to the stem cell expansion technology for cash and future royalties. The company plans to provide cell expansion services to cord blood banks and transplant centers throughout the U.S. and Europe as well as selectively licensing the technology to industry partners.

Success in cord blood transplants has been limited to babies and young children because of the small number of stem cells collected from umbilical cord blood, the company said.

"The patented technology acquired by A.I. could expand stem cells in cord blood that would be ample enough to treat adults who need bone marrow transplants," said Shai Meretzki, developer of the stem cell expansion process at the Technion.

* * *

Bioenvision Inc. (OTCBB: BIOV) of New York said it has signed a master services agreement with **Penn Pharmaceutical** for the labeling, packaging, storage and distribution of clofarabine in Europe.

Bioenvision also said it has initiated two phase II multi-center trials of the treatment to evaluate the efficacy in adult patients with acute myeloblastic leukemia and in children with acute lymphocytic leukemia.

The adult AML study, to take place at multiple sites in the U.K., will enroll 40 patients over the next

two quarters prior to interim analysis, the company said. The pediatric ALL study will take place in multiple sites in the U.K. and other E.U. countries. Both trials will be managed by RRD International, LLC and Tessman Technologies Ltd.

"The treatment options for older patients with AML are quite limited; the clinical need is great and we are enthusiastic about the opportunity to advance clofarabine as a potential therapy in this group," said Alan Burnett, principal investigator on the adult AML trial at the University Hospital of Wales in Cardiff.

Clofarabine is undergoing phase II trials in the U.S. for the treatment of acute leukemia in children and adults, and is also being evaluated in solid tumors, the company said. Clofarabine has been granted Orphan Drug Status in both Europe and the U.S. for Acute Lymphocytic Leukemia and Acute Myeloblastic Leukemia.

Clofarabine (Cl-F-ara-A, CAFdA) is a second generation purine nucleoside antimetabolite, which are antimetabolites that affect DNA synthesis, the company said. Clofarabine combines many of the favorable properties of the two most commonly used nucleoside analogs, Fludarabine Fludara by Schering AG (NYSE:SHR) and Cladribine, Leustatin by Johnson and Johnson (NYSE:JNJ), but is reported to have greater potency at damaging the DNA of Leukemia cells than the other agents., the company said. In a single center phase II study for refractory AML, 42 percent had a complete response rate and a further 13 percent had a partial response, the company said.

In another development, Bioenvision Inc. said it has entered into a general services agreement with **RRD International LLC**.

Under the agreement, RRD will advise and assist Bioenvision with its global development strategy and clinical trial design and management for its lead drugs, clofarabine and trilostane (Modrenal), as well as for its Oligon anti-infective technology, the company said.

Clofarabine is in phase II trials for acute leukemia in children and adults, and is also being evaluated in solid tumors, the company said. Modrenal is approved for marketing in the U.K. for advanced postmenopausal breast cancer. The company said it expects to begin U.S. clinical trials in prostate cancer in 2003. The Oligon antimicrobial material has been licensed to a third party for use in central venous and pulmonary artery catheters and is generating revenues, the company said.

* * *

Cytyc Corp. (Nasdaq: CYTC) of Boxborough, Mass., said it has entered into a multi-year collaborative sponsored research agreement with **Harvard Medical School** to discover molecular markers associated with the development and progression of neoplasia of the cervix, breast, and other organs.

Under the agreement, Cytyc would sponsor targeted research programs with two Harvard Medical School principal investigators, Peter Howley, head of the Harvard Medical School Department of Pathology, and Karl Munger, associate professor of pathology at Harvard Medical School.

"The collaboration will include an investigation of unique markers that may be present in the samples collected for the ThinPrep Pap Test and the FirstCyte Breast Test," said James Linder, vice president and chief medical officer at Cytyc. "We believe that coupling molecular markers with microscopic examination enhances the information that laboratories can provide to physicians."

Cytyc designs, develops, manufactures, and markets the ThinPrep System for medical diagnostic applications for cervical cancer screening and is the platform from which the company has expanded into breast cancer risk assessment with the FirstCyte Breast Test. The ThinPrep System consists of the ThinPrep 2000 Processor, ThinPrep 3000 Processor, and related reagents, filters, and other supplies.

In another development, Cytyc Corp. said it has entered into a new two-year agreement with **Quest Diagnostics** to market the ThinPrep Pap Test.

Quest Diagnostics first introduced the ThinPrep Pap Test in its labs in 1997, the company said.

Additional terms of the agreement were not disclosed, the company said.

In yet another development, Cytyc Corp. said the **American Society of Breast Surgeons** supports the use of ductal lavage as a cell-based risk assessment tool in high risk and borderline risk in making more informed decisions regarding risk reduction and management options.

"The American Society of Breast Surgeons believes that ductal lavage can play an important role in breast cancer risk assessment," said Shawna Willey, director of The Betty Lou Ourisman Breast Health Center, Georgetown University Medical Center, Washington, D.C. "The Society believes that identification of women at highest risk of developing breast cancer represents a very important initiative

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in our efforts to prevent this cancer."

The Cytyc FirstCyte Breast Test is a ductal lavage procedure that can be performed in an office setting in less than an hour, the company said. The cells collected with ductal lavage are analyzed in a laboratory to determine whether they are normal, premalignant, or malignant. Researchers have known for many years that the presence of atypical cells inside the breast milk ducts signals a significant increase in breast cancer risk, particularly for women with a family history of the disease.

* * *

FDA said it has established a cooperative research and development agreement with **Lincoln Technologies Inc.** of Wellesley, Mass., to develop tools for safety data mining.

The technology of data mining would enhance our ability to monitor the safety of drugs, biologics and vaccines after they have been approved for use, FDA said.

Data mining extracts information from large complex databases, the company said. The CRADA involves data that FDA already collects about adverse events involving approved drugs, biologics and vaccines. The specific data set used for data mining purposes does not include patient names, addresses, social security numbers or similar information.

Data collected from suspected drug-related adverse event reports and other electronic medical information could identify signals of adverse events and the patterns in which they occur, said FDA.

"Preventing adverse events associated with medical products is one of the FDA top priorities," said FDA Commissioner Mark McClellan. "By making greater use of state-of-the-art statistical tools coupled with 21st-century medical information systems, we can act more quickly and effectively."

FDA will continue to monitor the marketplace to ensure that products purporting to be dietary supplements are labeled properly and that claims being made for these types of products are not false or misleading.

FDA Center for Drug Evaluation and Research and Center for Biologics Evaluation and Research will work with Lincoln Technologies Inc., on the CRADA, said FDA.

"Through the use of enhanced data mining techniques we hope to improve upon our current ability to identify adverse event patterns in post-market safety databases," said Paul Seligman, the CDER principal investigator for the CRADA. Application of improved data mining tools has the potential for even earlier detection of safety signals associated with marketed products, especially adverse events from drug-drug interactions."

"The CRADA is intended to use modern computing and state-of-the-art statistical algorithms to sift through millions of suspected reaction reports and thousands of products to look for potential safety signals needing further scrutiny," said M. Miles Braun, CBER principal investigator for the CRADA.

* * *

ILEX Oncology Inc. (Nasdaq: ILXO) of San Antonio said it has agreed to license two research platforms focused on lipids to **QuatRx Pharmaceuticals** of Ann Arbor, Mich.

The platforms contain classes of orally active compounds that target the lowering of LDL Cholesterol and Lipoprotein (a), as well as target the elevation of HDL Cholesterol, the company said.

The compounds could be used as single agents or in combination with lipid-lowering drugs, the company said.

* * *

Mirada Solutions Ltd. of Oxford, U.K., and **R2 Technology Inc.** of Sunnyvale, Calif., have entered into a development and commercialization agreement to integrate the R2 OmniCAD platform and the Mirada Standard Mammogram Form technology to develop the next generation of CAD systems for mammography.

"Because the Standard Mammogram Form, or SMF, representation is intrinsic to the tissue characteristics of the breast, it is the optimal starting point to develop robust CAD applications that enhance the clinician's understanding of the mammogram image," said Christian Behrenbruch, CEO of Mirada Solutions.

SMF is a standardized representation of a mammogram computed from the image intensities (film or digital) and imaging parameters of the system used to acquire the image, the company said. The SMF standardization technology enables the optimization of mammograms acquired on different systems at different times for analysis, quantification and display.

ImageChecker system is approved for both film and digital mammography, the company said. The ImageChecker DM CAD system, pending FDA approval, is designed to offer an integrated solution to support CAD processing for analog and digital mammography.

* * *

OctoPlus of Leiden, The Netherlands and **CytImmune Sciences Inc.** of College Park, Md., said they have entered into a collaboration agreement to develop a tumor necrosis factor for solid cancers.

The TNF protein, the active agent in the treatment, has been shown effective against solid cancers, but also toxic, limiting its use, the company said. Using gold nanoparticles as a targeting drug delivery system, TNF will be delivered to tumors, the company said.

In animal model, it has been shown that by coupling TNF to very small gold particles, so-called colloid gold nanoparticles, less TNF is required for maximal anticancer action, reducing toxicity, the company said.

Under the agreement, the companies said they will develop a safer formulation to deliver more TNF to solid tumors and will evaluate the product in clinical studies, scheduled to start in early 2004. An undisclosed pharmaceutical partner will supply TNF for these studies.

* * *

Panacea Pharmaceuticals Inc. of Gaithersburg, Md., said it has formed a wholly-owned subsidiary, **Proteus Diagnostics Inc**., to develop and commercialize proprietary in vitro diagnostics including pharmacogenomic and pharmacoproteomic tools for cancer detection, diagnosis, prognosis, treatment selection, and follow-up.

Products developed by Proteus will be based on the enzyme human aspartyl (asparaginyl) beta-hydroxylase or HAAH, the company said. Panacea obtained exclusive, worldwide rights to all therapeutic and diagnostic uses of HAAH through license and collaborative research agreements with Rhode Island Hospital/Brown University in September 1999.

HAAH over-expression has been detected in more than 99 percent of 1,000 human tumor specimens from all 18 of the cancers tested to date and has not been detected in normal or unaffected, adjacent tissue, the company said.

* * *

PHASE-1 Molecular Toxicology of Santa Fe, N.M., said it is providing toxicogenomics services for NCI.

Toxicogenomics is the product of biotechnology and informational technology using human and animal genome data and advances in computer software for data archiving and mining, the company said.

"Toxicogenomics is a tool to define adverse drug toxicity," said Albert Li, president and CEO of PHASE-1. "The service we provide to NCI will aid the selection of potent anticancer drugs with minimal side effects and help define the mechanism responsible for toxicity."

PHASE-1 said it would receive animal tissues from multiple contract laboratories performing preclinical safety studies for NCI. The tissues will then be evaluated for treatment-related gene expression effects.

"The reason we went with PHASE-1 is that they have toxchips for the relevant species in which we perform our toxicity studies," said Joseph Tomaszewski, chief, Toxicology and Pharmacology Branch, NCI.

* * *

Plexxikon Inc. of Berkeley, Calif., said it has formed a drug discovery collaboration with **Genentech Inc.** (NYSE:DNA) to develop small molecule therapeutics for cancer.

Financial terms of the single target, multi-year agreement include an upfront technology access fee and research funding, a series of discovery and clinical milestone payments, and royalties on net product sales.

Under the agreement, Plexxikon will apply its Scaffold-Based Drug Discovery platform to develop a series of small molecule inhibitors against a single, undisclosed gene target in the protein kinase family, particularly implicated in oncology, the company said. Genentech will have an option to commercialize and market a series of compounds resulting from the collaboration under a worldwide license.

Development of the compounds, including clinical testing and manufacturing, will be the responsibility of Genentech.

* * *

Roche Diagnostics Corp. of Indianapolis, Ind. and **Sysmex Corporation of America**, of Long Grove, Ill., signed an asset purchase agreement enumerating the terms of a transfer of the Roche U.S. Hematology Business Unit back to Sysmex.

The agreement accelerates the expiration of an original distributorship, sales and service agreement that was due to expire in 2004, the company said.

"It was decided that both Roche and Sysmex would achieve greater success and profitability by focusing on their respective strengths," said Martin Madaus, president and CEO of Roche Diagnostics. "Both parties agree that for business reasons, it is best that the business be transitioned back to Sysmex."

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