THE CANCER LETTER

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Peers Puzzled By Herberman's Stance On Cell Phones While Believers Rally

By Paul Goldberg

A teaser for the Larry King Live news show July 29 got to the quintessence of the scientific controversy over cell phones:

"A prominent cancer researcher says, 'Put down that phone right now, if you want to reduce the risk of cancer!'"

The researcher in the spotlight was none other than Ronald Herberman, a respected immunologist and founding director of the University of Pittsburgh Cancer Institute.

A week earlier, Herberman stunned his colleagues by sending out an e-mail blast to his cancer center's 3,000 employees, urging them to limit their exposure to cell phones. This exploded into an international story: director of an NCI-designated cancer center sounds alarm over dangerous occupational exposure.

Meanwhile, Herberman's peers—including current and former directors

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In the Cancer Centers:

Fox Chase Names Jeff Boyd Scientific Officer And Makes Three Other Staff Appointments

FOX CHASE CANCER CENTER announced four recruitments. **Jeff Boyd**, of the Curtis and Elizabeth Anderson Cancer Institute and Memorial University Medical Center in Savannah, Ga., was appointed chief scientific officer at Fox Chase. Boyd is an international expert in translational research and has particular expertise in the genetics of breast, ovarian and endometrial cancer. He has helped define the role of tumor suppressors and oncogenes in these malignancies, most notably the p53, BRCA1 and BRCA2 tumor suppressor genes and their role in the development of breast and ovarian cancer. Boyd's most recent position was director of the Curtis and Elizabeth Anderson Cancer Institute and vice president of oncology and research at the Memorial University Medical Center. He also served as professor of medicine, surgery, obstetric and gynecology at the Mercer University School of Medicine, where he also was assistant dean of research. He also holds the title of Distinguished Cancer Scholar from the State of Georgia. Prior to his roles in Savannah, Boyd served a variety of leadership roles at Memorial Sloan Kettering Cancer Center. Prior to that, he held faculty positions at the University of Pennsylvania, the University of North Carolina and NIH. **Igor Astsaturov** joined the medical oncology staff, specializing in gastrointestinal cancers, including pancreatic, colorectal and neuroendocrine

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Herberman Plans To Study Long-Term Cell Phone Users

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of comprehensive cancer centers—say privately that they are watching with considerable surprise as the formerly cautious, conservative immunologist is staking his well-deserved, hard-earned prestige on a cause where data have been weak and findings cherry-picked.

"This whole thing makes no sense to me," said one prominent researcher. "What was the urgency?" asked another peer.

Scientists who know Herberman only by his publications were equally surprised. "I can't help but wonder just what on earth Dr. Herberman was smoking when he decided to issue this warning," David Gorski, a surgical oncologist at Barbara Ann Karmanos Cancer Institute, wrote on a quackbusters' blog called Science-Based Medicine. "Scaring the nation based on 'early unpublished data' that can't be examined by the entire medical and scientific community is generally not a good idea. That's why I've been asking over the last few days: Why on earth did Dr. Herberman do it?"

Otis Brawley, chief medical officer for the American Cancer Society, was similarly surprised. "I am afraid that if we pull the fire alarm, scaring people unnecessarily, and actually diverting their attention from things that they should be doing, then when we do pull the fire alarm for a public health emergency, we won't have the credibility for them to listen to us," Brawley said on the CNN show.

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By next year, Herberman is expected to leave the post of director institution he founded 23 years ago and become a scientist on the faculty. A search for his successor is underway. Recently, he told the Pittsburgh Post-Gazette that he planned to develop a research project focused on long-term cell phone users.

This would likely include analysis of usage data that may be obtained from cell phone companies. "The most important thing that I think could happen would be to try to induce the wireless cell phone industry to make their data available to independent research groups like the Center for Environmental Oncology within our cancer institute to actually analyze their data, which would [give us] a larger number of people to analyze than just the 9,000 from the Interphone study," Herberman said to The Cancer Letter last week.

While skeptics ponder Herberman's actions, believers in the hazards of cell phone use are elated. Devra Lee Davis, head of the UPMC Center for Environmental Oncology and an author of books claiming that environmental hazards are a major contributor to cancers, has been the primary beneficiary of Herberman's actions.

It was Davis, not Herberman, who appeared the Larry King show. Her book, titled "The Secret History of the War on Cancer," sat on King's desk.

The Secret History lays out much of the scientific justification for Herberman's alarm, and uses Herberman's life to illustrate the history of the government's assault on cancer and suggest that an environmental exposure had caused Herberman's chronic lymphocytic leukemia.

Herberman's late older brother Harvey also had CLL. "When two brothers from the same family with no known history of disease develop the same disorder of the blood and immune system, we have to ask, Is this just a coincidence," Davis hypothesizes in her book. "[Did] something happen to each of these men earlier in life to put them at risk of cancer?"

According to Davis's account, the younger Herberman has entertained the notion that his CLL was caused by an occupational exposure, when at age 19 he worked placing fish in beakers at the Museum of Natural History. "I anesthetized the fish with urethane, and as you know, urethane is a carcinogen in mice," he says, showing Davis an old photo of himself. "I handled the urethane and the solutions without gloves or any other precautions."

While skeptics may question the importance of environmental exposures as a cancer cause, in Pittsburgh, where extreme amounts of industrial chemicals have

been pumped into the air, ground and water for over a century, the hypothesis is well-received.

Indeed, one of the city's more prominent citizens, Teresa Heinz Kerry, is a major supporter of Davis's work. Records show that last year, the Heinz Endowment gave $317,370 to the University of Pittsburgh Cancer Institute for "funding to examine the correlation between environmental chemical exposures and epidemiological disease patterns, and to reduce their adverse biological effects." In 2006, the foundation gave Davis' center $250,000, and a year earlier, $150,000.

In a book she published last year, Heinz Kerry and husband Sen. John Kerry (D-Mass), praised Davis's work as well as the work of Rachel Carson, a crusader against industrial chemicals.

"The news that we are surrounded by an alphabet soup of toxic, unregulated chemicals may seem, at worst, alarming, and, at best, overwhelming," the Kerry's wrote in the book. "In response, Rachel Carson's words from Silent Spring are worth remembering: 'If, having endured much, we have at last asserted our right to know and, if knowing, we have concluded that we are being asked to take senseless and frightening risks, then we should no longer accept the counsel of those who tell us that we must fill our world with poisonous chemicals; we should look about and see what other course is open to us."

Also, the center receives funding from Genentech, the Milton Fine Foundation, the Caroline Fine-Friedman Foundation, the DSF Charitable Trust, the Highmark Foundation, the UPCI, NCI and NIHS. This year, the center's budget is over $1 million, Davis said.

What Einstein Knew In 1905

While Herberman's colleagues are concerned about his new public persona and while mainstream epidemiologists point to weaknesses in evidence, the Pittsburgh Post-Gazette has greeted Herberman's warning with great praise, calling it a "timely warning on possible cell phone danger."

Even before getting to epidemiology, skeptics point to a problem with the physics underlying Herberman's claims. Radiation emitted by cell phones isn't ionizing and therefore can't break chemical bonds. Robert Park, a University of Maryland physics professor who writes books about alternative medicine, described Herberman's claims as "nonsense."

"Einstein won the Nobel Prize in Physics for showing that cell phones can't cause cancer," Park wrote in his weekly dispatch called What's New. "The threshold energy of the photoelectric effect, for which Einstein won the prize, lies at the extreme blue end of the visible spectrum in the near ultraviolet. The same near-ultraviolet rays can also cause skin cancer. Red light is too weak to cause cancer. Cell-phone radiation is 10,000 times weaker."

While Davis points to images purported to show that "electromagnetic fields are likely to penetrate the brain more deeply for children than for adults," skeptics say, so what? The images appear on the Davis website: www.environmentaloncology.org/node/201.

Paul Song, a radiation oncologist and a believer in the Herberman warning, acknowledged on the Larry King show that existing physics doesn't justify concern about cell phones.

"For the radio waves, there has been no clear evidence to suggest that it's a DNA damage," Song said. "So if there is some damage, it has to be some other mechanism that has really yet to be reported."

Still, Song said that cell phone users should be concerned about their brains, eyes, and testes. "I think that an earpiece may help to greatly reduce the exposure for radio frequency radiation, but people need to keep in mind if the phone is on the hip pocket, their whole body is still being exposed to the same amount of radiation than if it was up to their ear," he said. "Surprisingly, the concern about radio frequency exposure is not so much for the brain or the hip, but really the testes or the eyes. Those are the areas that are most sensitive to radio frequency, because they get hot and they don't have the blood vessels to cool off."

What about television and hairdryers? asked Ted Schwartz, director of brain tumor surgery at New York Presbyterian Hospital/Weill Cornell, a skeptic.

"We don't know whether watching a television has an increased risk of causing cancer," Schwartz said. "We don't know whether using a hair dryer increases your risk of cancer. In fact, there are some studies showing there might be a link. But they're not well-performed studies, so we don't go around issuing public health warnings about it, based on the fact that we don't really have enough evidence. So I think it's a little premature to issue those kinds of warnings."

When a caller asked whether cordless phones are a concern as well, Davis answered in the affirmative.

"Well, there has been a study from Sweden where they have used cordless phones longer, and unfortunately what they found was that there was a doubled risk of a brain tumor with long use of cordless phones," she said. "And many cordless phones actually have as much radiation as a cell phone, if not more."

A transcript of the show is posted at http://

transcripts.cnn.com/TRANSCRIPTS/lkl.html.

"I don't get it," said the physicist Park, reflecting on the controversy. "Why would Ron Herberman, a law-abiding immunologist and stuffy administrator, who probably hasn't had a parking ticket in 20 years, suddenly decide to flout the most fundamental law of physics, the conservation of energy?"

Davis says this criticism is unfair. "Nobody ever said that cell phones are ionizing radiation or that they damage DNA," she said in an interview. "It's a completely fallacious argument. Can you tell me how smoking causes lung cancer? Do know that there are people still debating that?"

According to Louis Slesin, the editor of Microwave News, a newsletter covering health effects of non-ionizing radiation, France, Germany, the United Kingdom, and Israel urged consumers to limit children's exposure to cell phones. The Toronto Department of Public Health made a similar recommendation, Slesin said.

Seeing Signals or Cherry-Picking?

While Park speaks for the dominant view in science, a minority view, proposed by Tufts University researchers Ana Soto and Carlos Sonnenschein, describes carcinogenesis as a problem of tissue organization and comparable to organogenesis.

Applied to cell phone use, this theoretical approach may be verifiable through epidemiological studies. If these studies demonstrate an increased risk from non-ionizing radiation, this would disprove the dominant "somatic mutation" theory.

However, cell phone use notwithstanding, brain cancer incidence isn't on the rise. The rates increased in the 1970s and 1980s, before cell phones became commonplace, then started to decline.

In an interview last week, Herberman said that acoustic neuromas, benign tumors, have been observed in cell phone users and have been on the rise in the general population.

This is "very plausible, because these are tumors between the inner ear and the brain, and there is also data in the U.S. and in England that the incidence of acoustic neuromas has risen substantially over the last 20 years," Herberman said. "Of course, that's indirect correlation with the rising use of cell phones, but it at least is consistent with the possibility of the hazard, and could explain to a certain extent why the incidence has been rising."

Few mainstream epidemiologists agree with this analysis. According to a U.K. study published two years ago in the journal Neurology, the three-year moving average rates of acoustic neuromas rose from 2.4 cases per million in 1980 to 7.6 cases per million in 1997, then started to decline. In 2000, the three-year rates were at 5.5 per million.

"The trends in acoustic neuroma are most likely explained by changes in reporting and diagnosis," the British paper concludes (Nelson et al., Neurology 66, January 2006)). A Danish study that examined cell phone use between 1977 and 1995 reached a similar conclusion (M.F. Howitz et al, The American Journal of Otology, No. 5, 2000).

In the U.S., the incidence of acoustic neuromas is not rigorously measured, and is estimated at about 2,000 to 3,000 per year, said ACS's Brawley. "Accoustic neuromas are benign tumors, so until 10 or 15 years ago, no one in the U.S. has been counting them," Brawley said. "All databases that we have access to indicate that there is no rise in acoustic neuromas."

Overall, in the U.S., the incidence rate of malignant brain tumors rose from 50 cases per million in 1975 to 70 per million in 1987, and has been declining since. In 2005, it was 65 per million.

"We see this in the U.S. and Western Europe," Brawley said. "Brain tumor incidence went up because of availability of CTs, then started to decline, and are continuing to do so. We don't know why the rates are dropping, but we have looked hard, and we don't see evidence that cell phones are harmful."

Robert Tarone, biostatistics director of the International Epidemiology Institute, a Rockville-based think tank that was involved in interpretation of data from the Danish study, sees the same trend.

"Reports of increases in acoustic neuroma rates usually choose as their baseline 1970 or earlier; rates after 1990 are higher than they were in the 1960s and 1970s, but virtually all of the increase is in the mid- or late-1980s, after doctors started using CT and MRIs to diagnose brain tumors," said Tarone, who spent nearly three decades as a mathematical statistician at NCI before joining IEI,

"It's an example of detection bias, and this increase occurred before cell phones were widely used, and definitely before they had been used for 10 or more years, where some are now claiming there is an effect," Tarone said.

"Secular trends in acoustic neuroma rates have been published for several Scandinavian countries and for England and Wales, and they all show a similar pattern: tumor rates increased in the mid- or late-1980s, and then leveled off or decreased slightly after the rapid increase. A similar pattern has been observed for

childhood brain cancer in the US. It almost certainly reflects detection bias. Moreover, there was no long-term cell phone use in the 1980s, so the increase in acoustic neuroma rates can't be explained by prior cell phone use."

In addition to his position at IEI, Tarone serves as professor of medicine at the Vanderbilt University Medical Center and the Vanderbilt-Ingram Cancer Center.

Challenging the Danish Study

Preparing for the Larry King show, ACS staff put together a table of all studies of cell phone impact on brain tumors.

They found 14 case-control studies and three cohort studies. "All but three studies were unable to find an association between cell phone use and brain tumors," Brawley said to The Cancer Letter. The table is posted at http://www.cancerletter.com/publications/special-reports/special-reports.

Two of those positive trials were performed by the same researcher, Lennart Hardell, of Sweden. "The hazard ratios in those studies were well above 3.7. Given the extensive use of cell phones in Sweden, with those hazard ratios, we should be seeing an epidemic of brain tumors, which isn't happening," Brawley said.

Also, ACS staff went through Davis's website at Pitt (www.environmentaloncology.org/node/201) finding that the studies that don't support her approach are simply not mentioned. "This is an extreme case of selective use of data," Brawley said. "People who claim to be scientists should look at all the data, and their message should indicate that the data are inconsistent. We need to tell people what we know, what we do not know, and what we believe. Most importantly, we need to not confuse what we know with what we believe."

Davis said she is avoiding citing studies that aren't well designed. "It's not cherry-picking," she said. The case-control studies are "limited by the design of trying to study brain cancer people after they become sick. You are dealing with interviewing the patient or the next of kin. It's not that I don't cite them. I am not saying that they are evil people. I think that it's not the best kind of design under the circumstances."

Davis's efforts to raise doubts about cell phones start with a challenge to the Danish prospective cohort study that identified 420,095 cellular phone subscribers who received the phones between 1982 and 1995 and were followed through 2002.

The study found no association between cell phone use and brain tumors. "Moreover, the narrow confidence intervals provide evidence that any large association of risk of cancer and cellular telephone use can be excluded," concludes the study published in the Dec. 6, 2006, issue of JNCI.

What's wrong with the Danish study?

"The Danish study was designed to fail," Davis said in an interview. "Something like 70 percent of the cohort had short-term exposure."

That depends on what you call short. The mean time since the first telephone subscription was 8.5 years and the median was 8 years, the paper states.

"By definition, 50 percent of the cohort was followed for eight or more years," said Joseph McLaughlin, president of IEI and a former NCI epidemiologist. "We had 169,595 person-years of follow-up for 10 or more years after first subscription (i.e., the length of use for which claims are being made about tumorigenic effects) in the Danish cell phone cohort, and the standardized incidence ratio for brain and nervous system tumors was 0.66 with a 95% CI of 0.44-0.95. Thus, we found no evidence of tumorigenicity for the latency period that has been hypothesized to be of interest."

Also, the Danish study excluded telephones registered to businesses, Davis says. Indeed, 200,507 such phones weren't included in the follow-up "because the individual users could not be identified," the JNCI paper states.

"Come on, do you really think business cell phone users are going to use their cell phones less?" Davis said. "If you are a business user, you will be like my poor friend Andrea Martin, who ran her business from her car with her analog phone, or Johnny Cochrane, who his doctor told me was one of those glamorous first-time users and he couldn't be separated from the thing. Excluding your business users, you have a priori reasons for thinking that business users of cell phones are going to be using them more, not less."

Martin, founder of the Breast Cancer Fund, died of a brain tumor in 2003, and Cochrane, the Los Angeles celebrity lawyer, died of a brain tumor in 2005.

John Boice, scientific director at IEI, who joined the group after leading the NCI Radiation Epidemiology Branch, said he understands why Davis and her colleagues would focus on the study.

"This is the only cohort study, a prospective study, of cancer risk among cell phone users in the literature," said Boice, professor of medicine at Vanderbilt University Medical Center and Vanderbilt-Ingram Comprehensive Cancer Center, who is also an author on the two papers reporting outcomes of the Danish study.

"In all the others—Interphone and the other ones—participants were asked whether they had used a cell phone after their tumors had been diagnosed; their responses were compared with those of healthy controls who did not have brain tumors," Boice said. "We started with people who used cell phones and followed them forward to see what cancers they developed subsequent to their exposure. It is a superior research design."

The sample was large and the follow-up long. "The earliest date follow-up for cell phone use began was in 1982. So we had follow-up of up to 20 years, and the average follow-up was eight-and-a-half years," Boice said.

The authors discuss the exclusion of business users as a limitation of the study. However, they say they had no alternative to making the exclusion for the simple reason that businesses don't get brain tumors.

"It's unlikely to be a serious limitation," said Boice. "We could not identify specific people who used business phones. We only had the cellular phone subscriber lists. When the phones were tied to companies and businesses, there was no way to identify individual users—we just had a company.

"The business users may have been heavy users of cell phones. On the other hand, they may not have been. We don't know. I remember when I was at the NCI, I was assigned a cellular phone, and I used it about once a week."

Critiquing the Danish study in her book, Davis suggests that there is passive exposure to cell phone radiation. "Given how broadly cell signals now penetrate coffee shops, airports and some downtown areas of major cities, it is very difficult to find any truly unexposed groups against which to compare results," she wrote. "Because cell phone use has grown so fast and its technologies change every year, it is as if we are trying to study the car in which we are driving."

The passive exposure claim has no basis in science, said IEI's Tarone. "You have to have a cell phone very close to your head to have measurable microwave exposure of the brain, and even that exposure is relatively limited," he said. "So the argument that risk estimates for cell phone use would be attenuated because the entire population is exposed to microwave energy from cellular phone signals (as if cell signals were air pollution) is a diversion to muddy the water."

Wrangling Over Interphone Study

Another area of contention is the Interphone study, which has been bogged down for nearly two years.

While the countries have completed their work and some published their data, the overall results haven't been pooled, as was intended in the protocol.

"The study was completed and analyzed over two years ago," Herberman said to The Cancer Letter last week. "The frustration is, it has not been published yet. It's hard to point to it in a conclusive way. But I've talked with several people who are really experts, including biostatistics and epidemiology, and everyone I've talked to who has seen the data say there is clearly at least a two-fold increase in tumors on the side of the head where the cell phone tends to be used by somebody."

The release of the Interphone study data show that the vast majority of studies have found no correlation between tumors and cell phone use.

"A large number of the individual national components of the overall Interphone study have been published, and the results of most have been summarized on the IARC website," said Peter Boyle, director of the International Agency for Research on Cancer. "Most of the studies provide reassuring findings, although in some others there are hints of small increases at higher exposure levels. It is essential to see the pooled per-protocol analysis before drawing conclusions about any increased risk."

IARC oversees the central analysis of the 13-country trial that will cost over $15 million. However, the scientist who oversees the effort has left for the Center for Research in Environmental Epidemiology in Barcelona. Sources said that several investigators are claiming to see signals of harm from cell phones, while others say they do not.

"The investigators control the data and publication depends on all authors agreeing with the content of the final manuscript," Boyle said. "Currently there is disagreement between the authors on the interpretation of the study findings, with two groups holding divergent opinions. Given the importance of this study, surely the results should be published, enabling the scientific community to make up its own mind about the meaning of the study."

The delay can be entirely attributed to the dispute among investigators, Boyle said. "I am not aware of any external vested financial interests pressuring the conclusions of this study," he said.

Nearly all findings in the individual countries' studies have broad confidence intervals and nearly all encompass one. These studies should be analyzed together, said IEI's McLaughlin.

"In epidemiology, you look for consistency of results across all the studies, and you don't cherry-pick a particular study to find an increase of a particular type,"

he said. "In the German component of the Interphone study, there was an increased risk estimate in 10-year cell phone users for gliomas, but not for meningiomas or acoustic neuromas.

"When you look at the other Interphone studies, you do not find the elevated risk estimates after 10 years of cell phone use for glioma," McLaughlin said. "So what you see is random variations in risk estimates across all the studies, some estimates up and some down, and when you examine all the Interphone studies together, you find no consistent elevations for any particular type of brain tumor."

Like his IEI colleagues, McLaughlin is also a professor at Vanderbilt and its cancer center.

Some of the more concerning findings of the Interphone study are prone to bias, skeptics say.

"In the Interphone and other case-control studies, virtually all of the alleged effects have been found in analyses focused on the side of the head cell phones were used and the side of the brain the tumor occurred," IEI's Tarone said. "Some of these laterality analyses find increased risk estimates for cell phone use on the same side as the tumor, but decreased risk estimates for cell phone use on the side opposite the tumor."

To obtain this information, researchers ask patients how they used their cell phones after they were diagnosed with their brain tumors.

"When you examine those studies and look at acoustic neuroma analyses that ignore the side of the head, there is no evidence of increased risk," Tarone said. "It's only when they start asking, 'did you use the cell phone on this side or that side?' It may be a bias, because the patients know what side their acoustic neuroma was on and this may affect their reporting of laterality of cell phone use. And it can also be due to the fact that if they do use the cell phone on the side of the acoustic neuroma and the tumor starts to affect their hearing, which is often the first sign of an acoustic neuroma, their tumors may be detected earlier than in non-users or people who use cell phones on the opposite side from the tumor."

ACS President vs. ACS Staff

In an interview, Davis described skeptics at IEI as "an industry front group." The think tank "didn't disclose that their money came from the U.S. cell phone industry," she said. "Their money for this study [came from the industry.] They did outstanding work when they were at NCI, and the way they set up IEI was by a grant from the cell phone industry."

Turning to another matter, Davis said, "I think [IEI] has been a subject of a Congressional hearing for having failed to disclose that they were being paid by the coal industry. There have been a number of different things that this group has been involved in where they have worked for industry and not disclosed it, or where they have done work that other people find highly questionable. When I see some of the stuff they have done, I am disappointed."

These allegations surprised IEI President McLaughlin.

"This is all news to me," he said to The Cancer Letter. "We were never the subject of any Congressional hearing. I believe I would be aware of it if it were true. Watching C-SPAN is about as close as I've been to a Congressional hearing. We've never done a study for the coal industry. Our only connection to coal is Boice's deceased mother, who was a coal-miner's daughter from Pennsylvania. We have not done any studies for the cell phone industry, and we have never received any money from this industry. We did give some IEI funding to help complete the initial Danish study. This was a no-strings-attached contribution, and we proudly disclosed it in the JNCI paper in 2001. We have no secret funding at IEI. We disclose all funding in our publications."

Informed by a reporter about McLaughlin's reaction, Davis withdrew her allegations, blaming her confusion on stomach flu. "I want to take back everything I said about IEI," she said. "I have now gone back and realized that I made a mistake."

While the ACS staff has been firmly aligned with the skeptics, the charity's president Elmer Huerta has sided with Herberman and Davis.

"My position is much more assertive in terms of the public health recommendation," Huerta, a physician at the Washington Hospital Center who is also a broadcaster and blogger on health subjects in Spanish-language media, said to The Cancer Letter. "Even though we all agree that science is not there yet, but may be coming. The studies may come out positive by the year 2025 or 2030, so, are we going to just say, 'nothing's happened, let's wait for the studies,' and then face the future with something that is going to be catastrophic by the number of people that are being exposed to cell phones?"

Huerta said the ACS staff position reminds him of the society's reluctance 50 years ago to acknowledge that tobacco caused cancer. "This is déjà vu all over again with what happened with ACS with cigarettes," he said. "We need to conduct independent prospective research now. Meanwhile, I maintain my position for people to be cautious."

The ACS volunteer board hasn't taken a position on cell phone use, Huerta and Brawley said. Scientific issues of this sort are usually resolved by the society's professional staff, sometimes in consultation with outside experts. The staff recommendation, updated on May 28, is posted at www.cancer.org/docroot/PED/content/PED_1_3X_Cellular_Phones.asp.

Now, Huerta says that at the next ACS board meeting he would introduce a motion to endorse the University of Pittsburgh recommendation. His blog post on the subject is posted on the website of the Peruvian newspaper El Comercio: www.comercio.com.pe/cuidatusalud/2008/07/la-salud-y-los-telefonos-celul.html.

In the Cancer Centers:

Georgetown, Indivumed Agree To Expand Data Collaboration

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cancers. Astsaturov trained in immunology with a postdoctoral research fellowship at the University of Toronto and completed a three-year fellowship in medical oncology at Fox Chase. **Stephen Boorjian** joined the urologic oncology staff. He treats patients with prostate, bladder, kidney, testicular, ureteral, penile and urethral cancers. Boorjian came to Fox Chase after completing a fellowship in urologic oncology at the Mayo Clinic in Rochester, Minn. **Scot Ebbinghaus**, a medical oncologist specializing in lung cancer, recently joined Fox Chase. He was an associate professor of hematology and oncology at the University of Arizona and Arizona Cancer Center in Tucson. Ebbinghaus has served as principal investigator for several clinical trials involving patients with lung, kidney and other cancers. . . . **GEORGETOWN UNIVERSITY MEDICAL CENTER** announced an agreement with Indivumed GmbH, based in Hamburg, Germany. The arrangement builds upon a one-year agreement that established a tumor biobank and clinical database for pancreatic cancer and which now includes breast and colon cancer. The expanded collaboration will include a clinical database of prostate, glioblastoma, and renal cancer. The collaboration is a key step in the future development of the Georgetown Database of Cancer (G-DOC) at Lombardi Comprehensive Cancer Center at Georgetown. The G-DOC will be designed to combine clinical information from patients in clinical trials with molecular characteristics of their cancer. Indivumed is a privately owned company started by former Georgetown faculty member **Hartmut Juhl**. Indivumed also has partnerships with eight clinical cancer centers in Hamburg to collect similar specimens. . . . **CITY OF HOPE** announced two appointments. **Jay Thomas**, physician and research scientist in palliative care, was named chairman of its recently established Division of Supportive Care Medicine. Thomas will lead a division that unites palliative care and psychosocial support programs, such as patient support groups and clinical social work, under one multidisciplinary umbrella. **Laura Kruper**, breast cancer surgeon and researcher, was named assistant professor in the Department of General Oncologic Surgery. Prior to her appointment, Kruper completed a fellowship in breast cancer surgery at John Wayne Cancer Institute, Santa Monica, Calif.

In Brief:

AMERICAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY promoted **Dave Adler** to assistant director of government relations. Adler joined ASTRO in 2006 as government relations representative. **Richard Martin** was promoted to senior legislative and regulatory analyst. Martin came to ASTRO in February 2007 as a legislative and regulatory analyst. He monitors rulemaking of federal agencies.

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Business & Regulatory Report

Clinical Trials:

Bradmer Pharmaceuticals Begins Phase III Study Of Neuradiab For Glioblastoma

Bradmer Pharmaceuticals Inc. (TSX: BMR began enrollment in the phase III GLASS-ART Trial evaluating Neuradiab, a monoclonal antibody conjugated to Iodine-131, as a front-line therapy for primary glioblastoma multiforme.

The first patient was enrolled at the Preston Robert Tisch Brain Tumor Center at Duke University under direction of David Reardon.

"This trial culminates the extensive research we have performed at our institute over the years on Neuradiab, including seven peer-reviewed publications," said Reardon, lead principal investigator of the GLASS-ART Trial.

"We believe Neuradiab has broad applicability for patients with newly diagnosed GBM because the molecular target for Neuradiab, a protein called tenascin, is expressed in almost all GBM tumors," said Alan Ezrin, president

(Continued to page 2)

Deals & Collaborations:

GSK Releases Genomic Profiling Data For 300 Cancer Cell Lines Through caBIG

GlaxoSmithKline (NYSE:GSK) of Philadelphia said it has released genomic profiling data for 300 cancer cell lines through the NCI Bioinformatics Grid, or caBIG, that would save drug development time and capital for cancer research institutions.

The caBIG initiative is a network of infrastructure and tools that enables the collection, analysis, and sharing of data and knowledge.

"Cataloging this type of information in a network like caBIG leads to a ready-made body of biologic information that can be mined by all cancer researchers," said Richard Wooster, director of translational medicine oncology, research and development, GSK. "In turn, we hope the data will drive the identification of predictive biomarkers and lead to shorter, more directed clinical trials and faster drug development."

The genomic data come from cell lines derived from tumors, including breast, prostate, lung and ovarian cancers.

"The ability for researchers to share data via the caBIG network is exactly what this initiative was designed to enable," said Robert Clarke, professor of oncology and physiology and biophysics at the Lombardi Comprehensive Cancer Center, Georgetown University Medical Center and

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Phase III Study Of Neuradiab For GBM Begins Enrollment

(Continued from page 1)

and chief executive officer of Bradmer. "This stands in contrast to other agents under development for GBM which may only benefit a limited subset of patients for a variety of reasons. We look forward to bringing this investigational drug to patients via collaborative efforts with more than 30 U.S. cancer centers that are participating in the GLASS-ART Trial."

The phase III GLASS-ART Trial derives its name from its description: GBM Locoregional Agent Survival Study—Antitenascin Radiolabeled antibody Therapy Trial. The study is designed to determine the survival benefit derived from, and safety of, adding Neuradiab to the current standard of care therapy, consisting of surgery, radiation and adjuvant chemotherapy (temozolomide), for patients diagnosed with primary glioblastoma mulitforme. The randomized trial will enroll up to 760 patients at leading treatment centers across the U.S.

Neuradiab is a monoclonal antibody, conjugated to radioactive iodine. Neuradiab delivers tumor-killing radiation specifically to residual brain tumor cells after surgery, with minimal impact on normal brain tissue. During the course of development at Duke University, over $60 million in research grants and related support has produced a series of phase I and phase II clinical trials on Neuradiab and other closely related technologies.

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Approximately 200 brain cancer patients, including over 160 with GBM, have been treated with the Neuradiab therapy regimen, and survival benefits significantly exceeded historical controls in each completed trial. Neuradiab has been formerly referred to in literature as 131I anti-tenascin monoclonal antibody 81c6.

Genmab A/S (OMX: GEN) of Copenhagen said it has begun a 36-patient phase I/II study of zalutumumab (HuMax-EGFr) in combination with radiotherapy for advanced head and neck cancer that is ineligible for platinum based chemotherapy.

In the dose-escalation part, 6 to 24 patients will be enrolled in cohorts of 3 per dose level of the drug, the company said. The dose level for each successive cohort will be determined by the aggregate safety data observed in the prior cohorts. When the maximum tolerated dose of zalutumumab is established, an additional cohort of 12 will be enrolled and treated, the company said.

Treatment will consist of 8 weekly infusions of the agent, with the first cohort receiving an initial dose of 12 mg/kg of zalutumumab followed by 7 maintenance doses of 8 mg/kg of the product in addition to radiotherapy, the company said. Evaluation will occur at 4 weeks following the last dose of zalutumumab and patients will be followed for 2 years.

iCAD Inc. (NASDAQ:ICAD) of Nashua, N.H., said it has begun a clinical study for Colon CAD, its virtual colonoscopy CAD product, in partnership with **ACR Image Metrix.**

iCAD and ACR Image Metrix, having completed the development portion of the study, are collaborating on study execution including a multi- reader, multi-case clinical study to assess the impact of Colon CAD on the accuracy of interpreting CT Colonography exams, also known as virtual colonoscopies. The study will also assess the sensitivity of Colon CAD for detecting polyps and will measure the impact of the iCAD CT Colon CAD product on interpretation and workflow, the partners said.

The study, which will be managed and executed by ACR Image Metrix, will include 20 radiologists, and will incorporate the analysis of several hundred cases tested with virtual colonoscopy featuring Colon CAD.

"CT Colonography will not only provide a new and necessary option for cancer detection, but could increase screening rates nationwide," said Abraham Dachman, professor of radiology, University of Chicago Medical Center and principal investigator of the Colon CAD study. "While we expect the benefits in polyp detection

will be significant, we are also exploring how enhanced workflow features can add to the benefit CAD provides to CT Colonography."

ACR Image Metrix is a subsidiary of the American College of Radiology.

ImClone Systems Inc. (NASDAQ: IMCL) said it has begun enrollment in a phase II trial of IMC-A12, its fully human, IgG1 anti-insulin-like growth factor-1 receptor monoclonal antibody, in adolescents and adults with advanced soft tissue sarcoma.

The multinational 185-patient study would evaluate the efficacy of IMC-A12 in soft-tissue sarcoma types that include: Ewing's sarcoma, peripheral neuroectodermal tumor, rhabdomyosarcoma; leiomyosarcoma; adipocytic sarcoma, and synovial sarcoma. Based on supportive preclinical and biological rationale indicating that the IGF-1R and related signaling pathways may be overstimulated in the tumor types, and therefore sensitive to IMC-A12, the primary objective of the study is efficacy of IMC-A12 in adults and adolescents with the aforementioned subtypes of soft tissue sarcoma. The study will also characterize the safety of IMC-A12 as a single agent administered on an every-two-week schedule, the company said.

In addition to this study, phase II studies of IMC-A12 in advanced prostate, pancreatic, colorectal, liver, and head and neck cancers, as well as a series of phase I/II studies in pediatric malignancies and another evaluating the combination of IMC-A12 and temsirolimus, have begun enrollment, the company said.

In another development, ImClone said it has begun enrollment in a phase I study of IMC-A12, plus the mTOR inhibitor temsirolimus, in advanced solid malignancies and lymphoma at M.D. Anderson Cancer Center and Karmanos Cancer Institute, Wayne State University.

The study is a component of an initial stage of 10 phase I and II trials of the agent sponsored by the NCI Cancer Therapy Evaluation Program.

The phase I NCI-sponsored IMC-A12 trial is based on preclinical evidence that the mTOR and IGF-1R growth and survival signaling pathways are linked and, therefore, the combination of IMC-A12 and temsirolimus may optimize treatment, said Eric Rowinsky, chief medical officer and executive vice president of ImClone.

MethylGene Inc. (TSX: MYG) of Montreal said it has begun a phase II trial, Trial 013, evaluating MGCD0103, an isoform-selective histone deacetylase inhibitor product candidate, in combination with Vidaza (azacitidine for injection), a DNA demethylating agent, in high-risk myelodysplastic syndromes or acute myeloid leukemia.

The study is a three-arm, randomized 180-patient trial at cancer centers in North America and Europe.

"The trial can address a key question in the field of epigenetic cancer therapy: Is combination therapy with Vidaza and MGCD0103 superior to either agent alone?" said Charles Craddock, professor of Hemato-oncology, University of Birmingham, U.K., and an investigator for the trial. "Vidaza demonstrated a major survival benefit when used in high-risk MDS. The phase I/II data with this combination were also compelling, and we aim to determine definitively whether combination treatment is superior to monotherapy in MDS and AML."

Data from the 2007 phase I/II study for the combined use of MGCD0103 and Vidaza in MDS or AML demonstrated a 43 percent response rate (n=23) at the 90 mg dose with a median time to response of less than two months, the company said. The overall results indicated a 36 percent response rate evaluated at all doses (n=52 evaluable patients). The most common grade 3 and 4 non-hematological toxicities were fatigue and gastrointestinal in nature.

The recommended phase II dose for MGCD0103 was determined to be 90 mg, the company said. Vidaza did not affect MGCD0103 pharmacokinetics, nor did co-administration of compound impact the pharmacokinetics of Vidaza. A majority exhibited a substantial reduction in peripheral blood mononuclear cell HDAC activity during treatment with the combination.

MGCD0103 is an orally-administered, isoform-selective HDAC inhibitor, the company said. The compound is in multiple clinical trials: a phase I in combination with Taxotere for solid tumors; two phase I/II trials, the first in combination with Vidaza for hematological malignances and the second with Gemzar for pancreatic cancer; several phase II monotherapy trials in hematological malignancies and a phase II, three-arm combination trial with Vidaza in hematological malignancies, the company said.

Millennium began a phase I trial series of MLN4924, the company's first-in-class, small molecule inhibitor of the Millennium-discovered target, the Nedd 8 Activating Enzyme (NAE). MLN4924 advanced to the clinic with the first patient dosed in April.

The two phase I dose escalation studies aim to assess safety, tolerability, pharmacokinetic and pharmacodynamic effects in patients with advanced

solid tumors or with hematological malignancies.

The company also began a phase I hematologic trial of MLN8237, the first-in-class, specific Aurora A kinase inhibitor based on emerging pre-clinical data on the role of Aurora A in lymphomas and other hematologic tumors. Pre-clinical results also showed substantial activity in pediatric neuroblastoma and acute lymphocytic leukemia. Additional data related to the Aurora A kinase development program are scheduled to be presented at the 20th EORTC-NCI-AACR Symposium in Geneva, Switzerland in October. Millennium plans to expand the program to phase II trials in late 2008 or early 2009.

Monogram Biosciences Inc. (Nasdaq: MGRM) of South San Francisco said the HERmark Breast Cancer Assay would be available in the U.S. for assessment of HER2 status in breast cancer.

HERmark gives a precise and quantitative measurement of HER2 total protein and HER2 homodimer levels and will be offered as a CLIA-validated assay through the Monogram CAP-certified clinical laboratory, the company said.

"Breast cancer researchers and oncologists have come to agree that testing methods for HER2 are not adequate," said Peter Kaufman, associate professor of medicine at the Norris Cotton Cancer Center, Dartmouth-Hitchcock Medical Center. "The HERmark direct quantitative measurements of HER2 total protein and HER2 homodimer levels, provide much needed insight as to the real HER2 status of breast cancer. The technology may allow us to more accurately determine who will, and who won't, benefit from the use of Herceptin as part of their overall therapy."

With the measurements provided by HERmark, as many as 15-20 percent of patients determined by conventional technologies to be HER2-negative would be reclassified by HERmark, the company said.

Oncolytics Biotech Inc. (TSX:ONC, NASDAQ: ONCY) of Calgary said it is starting a phase II trial using intravenous administration of Reolysin in combination with paclitaxel and carboplatin in advanced head and neck cancers, in the U.S.

Monica Mita of the Cancer Therapy and Research Center, University of Texas Health Science Center in San Antonio, is principal investigator.

"Reolysin is one of the more exciting targeted agents under development in oncology," said Frank Giles, director of the Institute for Drug Development, Cancer Therapy and Research Center. "Our investigators within the CTRC at UTHSCSA are excited to study the synergy with standard cytotoxic agents and expand our studies into other tumor types and utilize other chemotherapy partner regimens."

The trial is a 14-patient, single arm, open-label, dose-targeted, non-randomized trial of the drug given intravenously in combination with a standard dosage of paclitaxel and carboplatin.

Eligible patients include those with advanced or metastatic head and neck cancers that are refractory to standard therapy or for which there is no curative standard therapy.

Progen Pharmaceuticals Limited (NASDAQ: PGLA) said it discontinued the PI-88 phase III study in liver cancer.

The company said the trial was unlikely to meet the forecast patient recruitment timetable and further significant delays were expected due to slower than expected regulatory processes in China, Korea and Vietnam; slower than expected initiation of clinical sites; slower than expected recruitment of patients into active sites; and the recent launch of a competitive phase III trial, assessing Bayer/Onyx Nexavar in the same indication.

Due to a lack of a global partner willing to meaningfully develop and commercialize PI-88, the commercial opportunity is much less than previously expected, the company said. These aspects would have delayed market entry.

The PI-88 trial had been facilitated through external agencies, and had resulted in 23 sites being opened for patient recruitment and 12 patients from 5 recruitment centers having been recruited to date. Existing patients receiving PI-88 will continue to receive the drug if they wish to do so, subject to regulatory approval. External costs of the trial in FY2008 are estimated at $9.8 million. The cost of discontinuing this trial is estimated to be less than $4 million.

Progen determined that the current phase IIb melanoma trial will be completed, but no further development in melanoma by Progen is anticipated at this stage. This trial is expected be finalized at an estimated additional cost of $300,000.

The company also decided to terminate further development of its phase I compound PI-166, based on a recent commercial assessment of the market and the approval of Nexavar in this indication. Progen said it will focus its resources on other compounds in development, PG11047 (phase I), the 500 series (late preclinical) and the epigenetics platform (early preclinical).

Deals & Collaborations:

GSK Releases Cell Line Data Through NCI's caBIG Network

(Continued from page 1)

Georgetown University Hospital. "As more scientists throughout the cancer community, in the U.S. and globally, use caBIG and find it easy to share data and collaborate, both basic and clinical research will be improved. This cancer cell data would be provided to other researchers and we also hope it will be a catalyst for other organizations to follow the GSK example."

NCI began the caBIG initiative in 2004 to accelerate approaches for cancer detection, diagnosis, and treatment. Since then, more than 40 biomedical research tools have been created, including caArray, the microarray data management system that is guiding the annotation and supporting the exchange of the cancer cell array data provided by GSK, the company said.

Barbara Ann Karmanos Cancer Center of Detroit said it has signed an agreement with **Meadowbrook C Management LLC**, to lease space and equipment at the Meadowbrook Medical Center in Novi, Mich.

The 14,000 square foot space will allow Karmanos to expand its outreach to cancer patients as well as provide access to radiation oncology, medical oncology and chemotherapy services. Under the agreement, Karmanos said it would see patients at this location in January.

GeneGo Inc. of St. Joseph, Mich., said **VTT Technical Research Centre** of Finland has licensed its MetaCore and MetaDrug in high-throughput compound screening, RNA interference experiments, cell biology and bioinformatics projects, to identify pathways and networks in translational cancer research.

VTT Medical Biotechnology Knowledge Centre in Turku has 85 researchers and staff members. The research is funded by the European Commission and the Academy of Finland. VTT accommodates two EU Marie Curie Centre of Excellence teams and coordinates the Academy of Finland Centre of Excellence for translational genome-wide biology, the company said.

OncoGenex Technologies Inc. of Vancouver and **Isis Pharmaceuticals Inc.** (NASDAQ:ISIS) of Carlsbad, Calif., said they have amended their agreement and OncoGenex has elected to independently develop its cancer drug OGX-011.

Under the amended agreement, OncoGenex is solely responsible for future development activities, costs and partnering decisions related to the drug, the companies said. Isis will no longer fund 35 percent of development costs, but will receive single digit royalties on future revenues of OGX-011, and will receive a portion of license fees and milestone payments received by OncoGenex from any future partner.

OncoGenex said it is conducting phase II trials of the product for hormone refractory prostate cancer. OGX-011 continues to show better than expected survival results when compared to published results, the company said.

The agent, also called custirsen sodium, is a second-generation antisense oligonucleotide that facilitates tumor cell death induced by chemotherapy by decreasing production of clusterin, a cell survival protein linked to treatment resistance, the company said.

Roche (Basel) and **Mirus Bio Corp.** (Madison, Wisc.) entered into a definitive agreement under which Roche will acquire Mirus Bio Corp., a privately-owned company based in Madison, Wisc., that focuses on the discovery and development of innovative nucleic acid based technologies, including a proprietary RNAi (Ribonucleic Acid interference) delivery platform.

In 2007, Roche announced a major alliance with the U.S.-based company Alnylam Pharmaceuticals Inc., which included the acquisition of Alnylam's European research site located in Kulmbach, Germany.

Under the terms of the agreement, Roche will fully acquire Mirus for $125 million and will maintain an RNAi research site in Madison. Mirus' transfection reagents business will be divested into a standalone business to be known as Mirus Bio LLC. Completion is expected during the second half of 2008.

Roche and **ARIUS Research Inc**. (TSX:ARI) said the two companies have signed a definitive agreement for Roche to acquire ARIUS in an all-cash transaction at a price of C$191 million.

ARIUS is the developer of an antibody platform called FunctionFIRST, which rapidly identifies and selects antibodies based on their functional ability to affect disease before progressing into clinical development. The platform will allow Roche to strengthen its developmental portfolio, initially within the areas of oncology and inflammatory diseases.

Rosetta Genomics Ltd. (Nasdaq: ROSG) of Rehovot, Israel, and Jersey City, N.J., said it is

collaborating with the **Rabin Medical Center** of Israel to develop microRNA-based diagnostics in oncology, gynecology and obstetrics.

The collaboration will use microRNAs as biomarkers to develop a range of diagnostic and prognostic tests, the company said. Rosetta Genomics said the collaboration is its first to include diagnostics for women's health indications.

MicroRNAs are naturally occurring, small RNAs that act as master regulators and could form the basis for a new class of diagnostics and therapeutics. Since many diseases are caused by the abnormal activity of proteins, the ability to selectively regulate protein activity through microRNAs could provide the means to treat a range of diseases, the company said.

Affiliated with the Sackler School of Medicine at Tel Aviv University, Rabin Medical Center is comprised of Beilinson and Hasharon Hospitals, and is one of the largest medical facilities in Israel.

Rosetta Genomics also said it has completed the acquisition of Parkway Clinical Laboratories Inc., a privately-held company owning a CLIA-certified lab located in Bensalem, Penn., for an aggregate purchase price of $2.9 million. The acquisition is expected to allow Rosetta Genomics to expedite development and validation of its microRNA-based diagnostic tests in the U.S. and worldwide. Ownership of the CLIA-certified lab will allow Rosetta Genomics to control the commercialization of its diagnostics, including marketing, sales, and reimbursement strategy.

TOPEX Inc. entered into a product distribution agreement with Radiology Oncology Systems, Inc. and **Acceletronics Inc**., for sales and service of its superficial radiotherapy system, the SRT 100, designed for the treatment of non-melanoma skin cancer.

The agreement provides for exclusive territory distribution in New York, New Jersey, Maryland, Delaware, Virginia, West Virginia, Ohio, Indiana, Kentucky, Missouri, and Pennsylvania. The territory outside the U.S. includes Mexico, Caribbean Countries, Central and South America.

The SRT 100 system provides an alternative to surgery for treating basal cell and squamous cell carcinomas, especially for primary lesions requiring difficult or extensive surgery with sensitive structures in the head and neck regions that would otherwise lead to a poor cosmetic outcome. The treatment does not require the use of anesthetics and eliminates the need for skin grafting when surgery could result in a less than desirable outcome, the company said.

Product Approvals & Applications:

FDA Grants Orphan Drug Designation To Epeius Product

Epeius Biotechnologies Corp. of San Marino, Calif., said Rexin-G has been granted FDA Orphan Drug Designation for soft tissue sarcomas and osteosarcoma.

Rexin-G, with its tumor-targeting nanotechnologies, has demonstrated single-agent efficacy in metastatic cancers of the colon, breast, skin, lung, and bone, the company said. Most recently, the product was approved in the Philippines for solid tumors that are refractory to standard chemotherapies.

Phase I safety studies established the general safety of Rexin-G, followed by phase I/II efficacy studies where optimal clinical protocols were established for each type of tumor, the company said.

AMDL (AMEX:ADL) of Tustin, Calif., said FDA has issued a letter of substantial equivalence to an existing predicate device and granted clearance to market AMDL-ELISA DR-70 as a safe and effective blood test to monitor colorectal cancer.

The clearance to market is the first that FDA has granted for any monitoring product for CRC since 1982 when Carcinoembryonic Antigen was approved, the company said. Until now, the CEA test has been the only accepted method cleared in the U.S. DR-70 offers a new test that can monitor CRC tumors post-surgery.

AMDL-ELISA DR-70: DR-70 is an Enzyme-Linked ImmunoSorbent Assay, or ELISA, is a diagnostic laboratory test that can be added to the pre-existing line of diagnostics, the company said.

Bayer HealthCare Pharmaceuticals Inc. of Wayne, N.J., said FDA approved Eovist (Gadoxetate Disodium) Injection, a gadolinium-based contrast agent, for intravenous use in T1-weighted magnetic resonance imaging of the liver to detect and characterize lesions in known or suspected focal liver disease.

Eovist is a paramagnetic MRI contrast agent that combines features of both an extracellular contrast agent and a hepatocyte-specific agent, the company said. Eovist is administered via an intravenous, bolus injection and has a dual route of excretion with 50 percent eliminated through the liver and 50 percent eliminated through the kidney.

"Eovist-enhanced images can provide more comprehensive information about focal liver lesions in a single, short imaging session than was previously

available," said Jeffrey Brown, professor of radiology, Washington University School of Medicine, St. Louis.

In the 816-patient trial, suspected or known focal liver lesions were enrolled in two of four non-randomized, intrapatient-controlled studies that evaluated the detection (studies one and two) or morphological characterization (studies three and four) of liver lesions. Studies one and two enrolled patients scheduled for liver surgery. MRI results were compared to a reference standard that consisted of surgical histopathology and the results from intra-operative ultrasound of the liver. The studies assessed the sensitivity of pre-contrast MRI and Eovist-contrasted MRI for the detection of liver lesions when each set of images was compared to the reference, the company said.

Studies three and four for known or suspected focal liver lesions included those not scheduled for liver surgery. MRI results were compared to a reference standard that consisted of surgical histopathology and other prospectively defined criteria. The studies assessed the correctness of liver lesion characterization by pre-contrast MRI and Eovist-contrasted MRI when each set of images was compared to the reference.

Lesions were characterized as one of the following choices: hepatocellular carcinoma, cholangiocarcinoma, metastasis, focal lymphoma, adenoma, focal nodular hyperplasia, hemangioma, abscess, focal liver fibrosis, regenerative nodule, focal fat, hydatid cyst, liver cyst, not assessable, normal, no lesion or other.

In all four studies, a baseline, pre-contrast MRI followed by the administration of Eovist at a dose of 0.025 mmol/kg body weight were given, with MRI performed immediately (the dynamic phase) and at 10 to 20 minutes following Eovist administration (the hepatocyte phase). Computerized tomography was done with contrast examinations of the liver. Pre-contrast MRI and Eovist-contrasted MR images were evaluated in a systematic, randomized, paired and unpaired fashion by three radiologists who were blinded to clinical information. Computed tomography images were also evaluated by the radiologists in a separate reading session.

The safety database was based on Eovist exposure in 1,755 adult subjects who received a dose that ranged from 0.003 to 0.5 mmol/kg body weight; the majority (N=1,365) received the recommended dose of 0.025 mmol/kg body weight.

Overall, 4.3 percent of subjects reported one or more drug-related adverse reactions during a follow-up period that, for most subjects, extended more than 24 hours after drug administration. The adverse reactions were mild to moderate severe. Serious adverse events were reported among six patients and were attributed to underlying conditions or non-MRI procedures. All serious events occurred more than 10 hours following Eovist administration. The most common adverse reactions at the recommended dose were feeling hot, nausea, headache, injection site reaction (pain, burning, coldness, extravasation), dysgeusia, flushing, parosmia, dizziness and vomiting.

Eovist is the first gadolinium-based, liver-specific MRI contrast agent, the company said. The product enhances the T1-weighted signal.

Eisai Corp. of Woodcliff Lake, N.J., said a supplemental biologics license application for Ontak was accepted for priority review by FDA.

The sBLA seeks to convert an accelerated approval indication into full approval, the company said. It is based on a placebo-controlled phase III l trial to confirm the clinical effectiveness of Ontak in cutaneous T-cell lymphoma.

The product is indicated for persistent or recurrent CTCL where malignant cells express the CD25 component of the IL-2 receptor. The safety and efficacy of Ontak in CTCL where malignant cells do not express the CD25 component of the IL-2 receptor have not been examined, the company said. Ontak was granted accelerated approval under Subpart E in 1999.

Genta Inc. (OTC Bulletin Board: GNTA) of Berkeley Heights, N.J., said it has received FDA notification to resume clinical trials with tesetaxel, an oral taxane.

The notification was made in response to the submission of a complete response to a prior notice from FDA that had placed the drug on clinical hold, the company said.

"FDA found that our initial submission addressed their safety concerns by incorporating careful monitoring and supportive care to reduce risks," said Loretta Itri, president, pharmaceutical development, and chief medical officer at Genta.

More than 250 patients have been treated with oral tesetaxel in phase I and phase II trials. The major side effect of tesetaxel in clinical trials has been myelosuppression, chiefly neutropenia. Due to the occurrence of severe neutropenia that led to fatal outcomes in several patients with advanced cancer, FDA placed the drug on clinical hold by FDA.

Millennium Pharmaceuticals of Cambridge,

Mass., **Takeda Oncology Co**. of Osaka and **Takeda Pharmaceutical Co. Ltd**., (TSE: 4502) said FDA approved Velcade for untreated multiple myeloma.

The co-development partner, Johnson & Johnson Pharmaceutical Research and Development LLC., also has filed a corresponding application with the European Medicines Evaluation Agency, the company said..

The approval was based on an international, multicenter, open label, active-control trial in untreated symptomatic multiple myeloma, the company said. Randomization consisted of either nine 6 week cycles of oral melphalan plus prednisone or MP plus Velcade. Antiviral prophylaxis was recommended for the Velcade study arm.

Time-to-progression was the primary efficacy endpoint. Overall survival, progression-free survival and response rate were secondary endpoints. A total of 682 patients were randomized: 338 to receive MP and 344 to receive the combination of bortezomib plus MP. The median age for both groups was 71 years. Demographics and baseline disease characteristics were similar between the two groups.

The safety profile of Velcade in combination with MP is consistent with the known safety profiles of both Velcade and MP, the company said.

Polyphenon Pharma said FDA granted Orphan Drug Designation to its botanical drug, Polyphenon E, for the treatment of chronic lymphocytic leukemia. A phase II study is currently underway at the Mayo Clinic in Rochester, Minn., where researchers are studying the effects of an oral daily dose of Polyphenon E in CLL patients.

Par Pharmaceutical Companies Inc. (NYSE: PRX) of Woodcliff Lake, N.J., said it has received final FDA approval for its Abbreviated New Drug Application for dronabinol, a generic version of the Solvay Pharmaceutical, Marinol, a CIII controlled substance.

The product is approved for nausea and vomiting associated with cancer chemotherapy when conventional antiemetic treatments failed and is available in 2.5mg, 5 mg and 10 mg strengths. Annual U.S. sales of Marinol are $190 million, according to IMS Health data, the company said. Par said it would begin shipment of all strengths of dronabinol soft gel capsules immediately.

Under the license and distribution agreement with SVC Pharma LP, an affiliate of Rhodes Technologies, Par said it has the right to market, sell and distribute dronabinol in the U.S. Par and SVC Pharma LP will share profits equally from the sales of the product.

SGX Pharmaceuticals (NASDAQ:SGXP) of San Diego said it has submitted an investigational new drug application to FDA for SGX393, its orally-bioavailable small molecule for relapsed and refractory chronic myelogenous leukemia.

SGX393 was discovered by SGX utilizing FAST, its fragment based approach to drug discovery, the company said. The agent fell within the purview of the SGX collaboration with the Novartis Institute for Biomedical Research, the company said. SGX obtained the right to further develop and commercialize the agent following an amendment to its agreement with Novartis that was signed in 2007, and it is subject to a reacquisition right of Novartis which may be exercisable at a future date.

Sound Pharmaceuticals has filed an Investigational New Drug Application with the FDA for the clinical testing of a proprietary formulation of ebselen for the prevention of chemotherapy induced hearing loss or ototoxicity.

The oral capsule containing ebselen, SPI-3005, will be tested in advanced stage lung cancer and head and neck cancer patients receiving platinum based chemotherapy. This marks the second development program for SPI to enter clinical testing for a hearing loss indication. Last year, SPI-1005, an oral capsule containing ebselen entered phase II testing with the U.S. Navy for the prevention and treatment of noise induced hearing loss.

Currently there are no FDA approved drugs for the prevention and treatment of drug induced hearing loss or ototoxicity.

Vermillion Inc. (NASDAQ:VRML) of Fremont, Calif., said it has submitted a 510(k) pre-market notification application to FDA requesting regulatory clearance of its ovarian tumor triage test, known as OVA1.

The OVA1 prospective clinical trial met its primary endpoints, indicating that the test is capable of stratifying women with pelvic masses into high- and low-risk categories to determine whether there should be referral to a specialist prior to surgery, the company said.

The trial, one of the largest ovarian cancer studies conducted, assessed 550 women with a confirmed adnexal mass at 27 clinical sites in the U.S. Additionally, the trial was the culmination of eight independent studies in 2500 women.