

# HCV ADVOCATE WEEKLY NEWS REVIEW

*Review of HCV, HBV and HIV/HCV Coinfection Related News and Highlights*

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**January 22<sup>nd</sup>, 2004**

### ***NIH Forming Conflicts-Of-Interest Panel***

*By RANDOLPH E. SCHMID  
Associated Press Writer*

WASHINGTON (AP) -- Reacting to reports that researchers received thousands of dollars as consultants with private firms, the head of the National Institutes of Health said Thursday he is forming a special task force to review such relationships for possible conflicts.

Dr. Elias A. Zerhouni told the Senate Health and Human Services appropriations subcommittee that he will ask the panel to report in 90 days on what types of collaboration are appropriate and to make recommendations for any rules changes that may be needed.

The subcommittee called in Zerhouni to respond to reports that some NIH scientists have been paid thousands of dollars in cash and stock to serve as consultants. He did not discuss specific cases other than to say they were under review.

But Zerhouni stressed that under rules changes made in 1995, NIH scientists are allowed to consult with private firms on projects that are not part of their direct government research work. He said his office is currently reviewing the 365 such collaborations currently in effect to make sure they follow the rules.

Crossover between NIH researchers and the private sector is important to move basic research into treatments that improve health, he said, "but in that process the people at NIH need to have absolutely clean hands."

Sen. Arlen Specter, R-Pa., said he feels the relationships could pose a substantial problem that needs to be investigated, particularly if a scientist collaborates with one company to the exclusion of others.

But Sen. Ted Stevens, R-Alaska, stressed the benefits of government-industry relationships, commenting, "I believe we need to encourage collaboration rather than putting some sort of taint on it."

Zerhouni said no new approvals for outside consulting will be issued until the new committee completes its study.

He said the approximately 200 scientists with approved consulting arrangements represent about 3 percent of the agency's researchers. None of the NIH's institute directors have consulting agreements, he said.

Zerhouni's office later announced that the new review panel will be headed by Bruce Alberts, a biochemist who is president of the National Academy of Sciences, and Norman R. Augustine, chairman of the executive committee of Lockheed Martin and former head of the National Academy of Engineering.

Marilyn L. Glynn, acting director of the Office of Government Ethics, told the panel that her agency conducts periodic ethics reviews at government branches and is currently doing one at NIH.

The review will focus on the structure of NIH's ethics program, the public financial disclosure system and the process for approving outside activities, she said.

The last NIH review, in 2000, found that a new ethics official at the National Institute of Diabetes, Digestive and Kidney Disease could not locate approvals for outside activity granted before he took the position, Glynn said in testimony. She said that has been corrected.

Dr. Stephen I. Katz, director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases, said in testimony that he previously had done outside consulting but had terminated the one remaining agreement in November.

The consulting arrangements generally involved his critiquing company programs to address specific scientific issues, said Katz, who was been a focus of reports on NIH scientists' outside work.

"In no instance did I ever discuss, with any company with which I was consulting, any research that it might be conducting with the NIH or any application it might have submitted to NIH for funding," he said in testimony.

On the Net:

National Institutes of Health: <http://www.nih.gov/>

Source: *Associated Press.*

**January 24<sup>th</sup>, 2004**

## ***Many Civil Suits Now Filed***

*By Beverly J. Lydick/Tribune staff*

In October 2002, Nebraska Department of Health officials created an emotional firestorm in the Fremont area by asking more than 600 people to be tested for a strain of hepatitis C.

State officials issued 612 letters suggesting the screening after a cluster of people identified as having hepatitis C, genotype 3A, were discovered to have been under the care of Dr. Tahir Javed and the Fremont Cancer Center.

Officials surmised an individual who had received care at the center was hepatitis C positive prior to seeking treatment, and may have introduced the disease to the facility.

Dates of exposure were narrowed to between March 1, 2000, and Dec. 31, 2001.

The announcement quickly grabbed the attention of the general public, with print and broadcast journalists descending on Fremont to cast light on what would come to be known as "the largest hepatitis C outbreak of its kind in the nation."

Of the 612 cancer patients who received that initial notification from the health department, 485 chose to be screened for hepatitis C. Initially, 82 tested positive for the virus.

Following those results, several patients filed claims of malpractice against the clinic and Javed.

On March 7, a 49-year-old woman who had tested positive for hepatitis C died in an Omaha hospital while awaiting a liver transplant.

As the community struggled to deal with rumors and misinformation about the virus and its effects, support groups formed. A public forum was held March 16, drawing state and federal medical officials - and about 100 citizens.

In June, following a second round of tests, another 17 cases of the virus were detected among Javed's former patients. In all, 99 people tested positive for hepatitis C genotype 3a. The state

health department ultimately blamed unsanitary medical procedures at the cancer clinic for the epidemic.

By August, 81 lawsuits filled a shelf in the office of the Dodge County District Court Clerk. Most named as defendants Javed, his nurse Linda Prochaska, Dodge County and the Fremont Area Medical Center, the county-owned facility where the oncologist's office was located.

On Oct. 1, the state pulled Javed's license to practice medicine in Nebraska. The doctor, who left the state in July 2002, currently serves as a minister of health in his native country of Pakistan.

By January of this year, 99 civil suits had been filed in district court. On Jan. 16, District Court Judge John Samson announced the first case would not be tried until at least January 2005.

*Source: Fremont Tribune*

**January 26<sup>th</sup>, 2004**

### ***A National Survey of Split-Liver Transplantation in the United States***

*Source: [www.gastrohep.com](http://www.gastrohep.com)*

Biliary and vascular complications account for the majority of morbidity in split-liver transplantations, find researchers in the February issue of *Annals of Surgery*.

Split-liver transplantation is a theoretically attractive mechanism to increase cadaver organ supply. In this study, a team of researchers assessed the application and outcomes of split-liver transplantation in the United States.

They surveyed 89 surgical teams between 2000 and 2001. The researchers collected data on graft type, recipient status, procurement method, graft sharing, graft outcomes, recipient outcomes, and experience with whole-organ transplantation.

Of the 89 surgical teams, 83 provided the researchers with data on 207 left lateral segment, 152 right trisegment, 15 left lobe, and 13 right lobe grafts.

The research team established that the split procedure was performed ex vivo in 54% and in situ in 46% of grafts.

They determined that complications occurred frequently in all graft types. Biliary and vascular complications were evenly distributed between grafts procured by either technique.

The researchers found that primary nonfunction, graft failure, and recipient death correlated with transplant status.

Dr John Renz's team concluded, "Split-liver transplantation has been principally applied to adult-child pairs with at least one recipient critically ill".

"Biliary and vascular complications account for the majority of morbidity in grafts procured by either split technique with graft failure and recipient death observed more frequently in critically ill recipients".

"Enhanced utilization and improved results may be possible through improved information sharing and modification of allocation criteria".

*Ann Surg 2004; 239(2): 172-81*

## **Schering-Plough CEO: Consent Decree Lasts Through 2005**

*Hollister H. Hovey*

NEW YORK (Dow Jones)--There are still too many moving parts in Schering-Plough Corp.'s (SGP) business to offer specific 2004 guidance, Chairman and Chief Executive Fred Hassan said Monday on the company's fourth-quarter conference call.

However, the beleaguered drug maker still expects 2004 to be worse than 2003, he said, echoing previous statements that the company won't start to see a turnaround until 2005.

It's unclear if that means that Schering-Plough will be in the red in 2004. In 2003, the company swung to a loss of \$92 million, or 6 cents a share. But that included \$350 million to increase litigation reserves and charges related to a voluntary retirement program. In 2002, Schering-Plough had profit of \$1.97 billion, or \$1.34 a share.

Hassan's outlook that 2004 will be worse than last year doesn't include any charges like the \$350 million charge it took in 2003.

The company is suffering from a massive decline in sales in its allergy franchise since Claritin lost patent protection in 2002. Its hepatitis-C franchise has also seen big declines since Roche launched a competitor and the market for these drugs shrunk as a whole. One of the drugs in the hepatitis-C group, Rebetol, faces generic competition imminently, so the company has been trying to get rid of extra inventory.

The company also remains under the eye of the Food and Drug Administration with a consent decree in effect until December 2005. The company has to satisfy the FDA's concerns about its manufacturing by certain dates or will face fines. So far, the company has completed 91 significant steps of the consent decree, Hassan said. There are 129 more to go, he added. The company didn't have to pay any fines for missteps in 2003, he said.

At the same time, the company is getting ready to launch a cholesterol pill that combines its drug Zetia with Merck & Co.'s (MRK) Zocor. It will increase promotional spending for that drug and Zetia itself in 2004.

So, to save money - the company wants to find more than \$200 million in cost savings - there will be more layoffs this year. In 2003, 900 people out of the 2,400 who were eligible, opted to take early retirement. Schering-Plough's goal is to cut 10% of its payroll expenses.

Cost cuts will come from all over the company, except in areas covered by the consent decree and sales force.

Schering-Plough swung to a fourth-quarter loss, as it saw those key franchises decline, lost revenue from AstraZeneca PLC (AZN) as its alliance with heartburn drug Losec ended and the company paid charges related to that voluntary retirement program.

Earlier Monday, the Kenilworth, N.J., company said its fourth-quarter loss was \$181 million, or 12 cents a share. The loss included \$179 million of employee termination costs, mostly from a voluntary early retirement program, and asset-impairment charges of \$50 million.

Excluding items, the company reported fourth-quarter income of a penny a share. Schering earned \$313 million, or 21 cents a share, for its year-ago fourth quarter.

Fourth-quarter sales fell 18% to \$1.95 billion from \$2.37 billion last year, slowed by sales at the Intron franchise, which includes the anticancer/antiviral agent Intron A Injection, as monotherapy and in combination with Rebetol capsules for treating hepatitis C, and Peg-Intron Powder for Injection, a longer-acting form of Intron A, as monotherapy and in combination with Rebetol for treating hepatitis C.

Analysts surveyed by Thomson First Call were expecting Schering to earn 4 cents a share on sales of \$2.03 billion for its fourth quarter.

Hassan said that in the future, the company, which has been a powerhouse in allergy and cholesterol drugs, will start to refocus on oncology.

### ***Rigel Pharmaceuticals, Inc.'s (RIGL) R803 for HCV Achieves Favorable Safety Profile***

SOUTH SAN FRANCISCO, Calif., Jan. 26 /PRNewswire-FirstCall/ -- Rigel Pharmaceuticals, Inc. today announced positive clinical safety data from a Phase I trial for R803, an experimental drug to treat Hepatitis C Virus (HCV), the blood-borne virus that affects nearly 170 million people worldwide. Clinical data indicates that R803 is well tolerated with no notable adverse effects reported in the dose levels that Rigel plans to use moving forward. Rigel plans to launch a Phase I/II efficacy clinical trial in the U.S. during the second quarter of 2004 in HCV-infected patients. This trial will monitor viral clearance and safety over numerous days of drug administration.

In the Phase I trial, an escalating dose regimen of R803 was studied in 42 volunteers and was compared with placebo controls. The safety data collected indicated that subjects treated with R803 were indistinguishable from the placebo controls across a wide range of clinical and laboratory safety tests, including clinical signs and symptoms, serial electrocardiography, and clinical chemistry and hematology studies. Pharmacokinetic data, which will aid in planning dosing in the next clinical study, was also collected. The trial was conducted in the U.K. and the results will be part of the U.S. IND package that Rigel expects to file with the FDA later in the first quarter of 2004.

"A leading issue for the millions of Americans infected with chronic HCV are the side effects of current therapies and their relatively limited efficacy," noted Jules L. Dienstag, M.D., Professor of Medicine and Associate Dean for Academic and Clinical Programs at Harvard Medical School and a steering committee member of the upcoming study. "R803 continues to show promise as a unique first-line anti-HCV therapeutic, directly targeting HCV by interfering with the viral polymerase protein that is needed for replication."

"The successful completion of Phase I safety trials represents another major step in Rigel's efforts to advance the clinical development of R803," said Elliott Grossbard M.D., Senior Vice President, Medical Development. "The availability of a new oral therapy that is convenient, safe and effective would be an important addition to currently available treatment options for patients with HCV."

Rigel's R803, a non-nucleoside HCV polymerase inhibitor, is an oral, small-molecule compound. To date, R803 has demonstrated potent efficacy in inhibiting viral replication in cell-based assay systems and in live virus assays. R803 has been shown to be efficacious against various genotypes of HCV, including genotype 1, the most common in North America and Europe. In various assays, R803 appears to act within days to reduce viral levels significantly. In addition, as a result of R803's novel viral binding site, resistance may be slow to develop.

#### *HCV: Current Treatments and Market Opportunity*

Hepatitis C is an inflammation of the liver caused by the hepatitis C virus. As the most common blood-borne infection in the U.S., HCV affects 4 million Americans and 170 million individuals worldwide. Approximately 85 percent of those with acute illness will go on to develop chronic hepatitis, a condition that has been linked to cirrhosis, hepatocellular carcinoma (liver cancer) and liver failure. HCV accounts for 30 percent of end-stage liver disease and liver cancer and is the leading cause of liver failure, which can result in the need for liver transplantation. Public health officials in the U.S. and abroad have mobilized to address this medical crisis by identifying detection guidelines for HCV and implementing therapies to eradicate chronic infection.

Currently available HCV therapies are only modestly effective at treating the disease. The most prevalent treatment regimen is with interferon alpha (IFN), usually in combination with ribavirin. IFN shows only a 20 percent to 40 percent success rate in patients who complete therapy, and significant side effects result in up to half the patients either quitting treatment or moving to a lower dose regimen. Moreover, IFN is least effective against HCV genotype 1, the strain responsible for 70 percent of chronic HCV infection cases in the U.S. Rigel believes that its approach is substantially different than that of IFN: instead of working to boost the immune system, experiments indicate that R803 directly, rapidly, selectively and potently targets HCV by interfering with a viral polymerase protein that is needed for replication.

With the current high prevalence and projected increase in cases of HCV and related diseases, and with the limited success of currently available therapies, Rigel believes that the potential for new direct HCV therapeutics is large and that R803 has the potential to be at the forefront of this opportunity.

*About Rigel (<http://www.rigel.com/>)*

*Rigel's mission is to become a source of novel, small-molecule drugs to meet large, unmet medical needs. Rigel has identified four disease areas with which to focus its lead product development programs: asthma/allergy, virology, immunology and oncology. Rigel has begun clinical testing of its first two product candidates, R112 for allergic rhinitis and R803 for hepatitis C, and plans to begin clinical trials of two additional drug candidates, for the treatment of rheumatoid arthritis and asthma, by the end of 2004.*

This press release contains "forward-looking" statements, including statements related to Rigel's plans to pursue clinical development of drug candidates and the timing thereof and the potential efficacy of drug candidates. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "plans," "intends," "expects" and similar expressions are intended to identify these forward-looking statements. There are a number of important factors that could cause Rigel's results to differ materially from those indicated by these forward-looking statements, including risks associated with the timing and success of clinical trials and the commercialization of product candidates, as well as other risks, detailed from time to time in Rigel's SEC reports, including its Quarterly Report on Form 10-Q for the quarter ended September 30, 2003 and Annual Report on Form 10-K, as amended, for the year ended December 31, 2002. Rigel does not undertake any obligation to update forward-looking statements.

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Web site: <http://www.rigel.com/>

Source: *BioSpace*

## **Novartis Resumes Merger Search; Talks Up Schering, Ups Stake In Roche**

Novartis is resuming its search for a merger partner, CEO Daniel Vasella indicated during the company's 2003 results conference Jan. 22 in Zurich.

Vasella encouraged speculation about Novartis' plans by offering a pointed non-answer to a question about the company's potential interest in Schering-Plough.

"As to specifics, I would not comment," Vasella responded. "But, that is very interesting, I would say."

Novartis attempted to pull off an acquisition at the end of the 1990s with the goal of boosting its U.S. presence ahead of a string of expected product launches. The company submitted a bid for Monsanto/Searle but was rejected; Pharmacia subsequently acquired Searle and then merged into Pfizer.

In 2001, Vasella announced that the company felt the time had passed for an acquisition and said it would "prefer" to wait for two or three years before making its next move ("The Pink Sheet" May 7, 2001, p. 19).

True to his word, Vasella is kicking off 2004 by stirring up speculation about Novartis' aims.

He pointed out that the dynamics of the international equity markets play to the advantage of Novartis.

"For a European company, a U.S. company currently with the low dollar has become less expensive," he said.

However, Vasella added, "I do not think that anybody would be foolish enough to just buy a company because it is less expensive."

"In the long run, if it is the right acquisition or the right merger, people tend to forget the price and they remember if the result is good or bad," Vasella said.

In analyzing a merger, Novartis will ask: "What is the product portfolio, the pipeline, the area of activities, and the geographic fit?" Vasella said.

"It is a cold, fact-based analysis which is different for different companies as they look at a certain partner or target."

"As to specifics," he concluded, "I would not comment. What is really interesting, I won't say."

Novartis has clearly indicated its interest in one potential merger partner: Swiss neighbor Roche. Novartis purchased a 21.3% stake in Roche in 2001 and upped the stake to 32.7% in 2003 ("The Pink Sheet" Jan. 27, 2003, p. 22).

Novartis raised its stake in Roche to 33.3% in the fourth quarter, although Vasella characterized the added investment as "irrelevant."

"We think it is a good investment and we are very appreciative of their turnaround and the success they have now," he said. "If we were to go beyond 33.3% that would be worth mentioning because then we would have to make an offer for the entire company under Swiss law."

One interpretation of Vasella's comments on possible interest in Schering-Plough is that it is another attempt to put pressure on Roche's controlling shareholders to consider a deal.

It is unlikely that Novartis would acquire both Schering and Roche, given the two firms' competitive position in the interferon market. By encouraging speculation that it is interested in Schering, Novartis is also reminding Roche's owners that it has other options.

The political appeal of a Roche/Novartis merger could increase if the speculation about a French mega-merger between Sanofi and Aventis comes to fruition (see preceding story).

A Sanofi/Aventis merger would also bump Novartis farther down the ranking of global pharma companies. Novartis began operations following the Ciba/Sandoz merger as the world's largest pharmaceutical company.

It currently ranks fifth, behind Pfizer, GlaxoSmithKline, Merck and Johnson & Johnson.

Whether or not Novartis steps up to make an offer for Schering, Vasella's comments are sure to renew speculation about Schering's future.

Nine months into the tenure of CEO Fred Hassan (who led Pharmacia's successful bid for Searle), Schering is showing the first signs of a turnaround.

At the very least, Schering appears to have reached the point where potential suitors could feel comfortable putting a value on the company.

The impact of the Claritin OTC switch is now clear, the company says it has "stabilized" market-share losses for other products, and the launch of the cholesterol agent Zetia has given the company a potentially attractive new product.

Schering's product line appears to be a good fit for Novartis in the U.S. Schering's strengths in asthma/allergy, oncology/virology and cholesterol would complement Novartis' line. The two companies would also have a strong combined presence in the OTC market.

However, there are also several potential obstacles to bids for the company. First, Zetia is tied up in a joint venture with Merck, and the "change in control" provisions would allow Merck to buy out the joint venture if Schering enters into any merger where its shareholders retain less than 40% ownership ("The Pink Sheet" Nov. 4, 2002, p. 6).

In addition, Schering is facing potential criminal charges stemming from an investigation of its marketing and pricing practices.

The company has so far reserved \$500 mil. to cover potential liabilities in the criminal case, spearheaded by the Boston U.S. Attorney, and another investigation led by the Philadelphia U.S. Attorney ("The Pink Sheet" March 3, 2003, p. 4).

Finally, any potential suitor for Schering may have difficulty wringing significant synergies out of the company.

Hassan has initiated some steep cuts in Schering's expenses - sparing only the sales force and employees necessary to the firm's Good Manufacturing Practices consent decree with FDA ("The Pink Sheet" Aug. 25, 2003, p. 15).

**January 27<sup>th</sup>, 2004**

### ***Hepatitis C Infection Early in Life Rarely Serious***

*Source: Reuters Health*

NEW YORK (Reuters Health) - Hepatitis C (HCV) infection acquired early in life rarely, if ever, progresses to the liver-scarring disease cirrhosis, new research suggests.

HCV infection during adulthood is associated with a higher risk of progression to cirrhosis within 20 years than that acquired earlier in life, senior investigator Dr. Alessandro Remo Zanetti and colleagues note in medical journal *Hepatology*. However, most studies of disease progression rarely encompassed more than 20 years of follow-up.

To gain further insight into outcomes of HCV infection, Zanetti, at the University of Milan in Italy, and his group identified 31 individuals who, as children in 1968, had received blood from donors later found to be infected with HCV.

The researchers obtained blood samples from these subjects in 1998, and found that only 18 had any evidence of infection. Although mild liver damage was noted in a few subjects on follow-up 5 years later, none had cirrhosis.

"Taking into account the limited study sample," the authors conclude, "these findings suggest that HCV infection acquired early in life shows a slow progression and mild outcome during the first 35 years of infection."

*SOURCE: Hepatology, January 2004.*

## **Reported Hepatitis Cases on the Rise in Parts of Pennsylvania**

*Joann Loviglio  
Associated Press*

CDC figures show that reported acute cases and new infections of hepatitis C dropped more than 50 percent nationwide from 1980 to 2002. But the Pennsylvania Department of Health's (PDH) statistics show the total number of hepatitis cases in Luzerne County rose from 32 in 1993 to 67 in 2001.

PDH's annual County Health Profiles list only hepatitis A and B, two of five recognized strains of the disease. But Wilkes-Barre physician Robert Czwalina went from treating one patient with hepatitis C to treating 30 within a year. He said changing demographics, notably people with drug and alcohol problems who acquire hepatitis C elsewhere and move to rural Pennsylvania, account for the rise.

State regulations that took effect last year require health professionals to report all cases of hepatitis including the three most common US strains: A, B and C. Reported cases of hepatitis A and B increased only moderately in Pennsylvania from 1994-2001: 903 to 1,097 for hepatitis A and 829 to 864 for hepatitis B.

In York, hepatitis C cases jumped from 10 in 1999 to 105 in 2003. Health officials believe the rise comes from improvements in health care rather than changing demographics.

Dr. David L. Hawk, director of the York City Bureau of Health, said greater awareness of hepatitis in the medical community, more testing and better reporting account for the rise in cases, and that the increase in hepatitis B and C represents people who have had the virus for years.

Whether the numbers come from a changing population or more vigilant doctors, health professionals agree that there is too little money for drug and alcohol treatment and medication.

## **Hepatitis B Virus Reactivation in Breast Cancer Patients**

*Source: [www.gastrohep.com](http://www.gastrohep.com)*

A high hepatitis B viral load before cytotoxic chemotherapy is a significant risk factor for the development of HBV reactivation, find doctors in the January issue of the *Journal of the Viral Hepatitis*.

Hepatitis B virus (HBV) reactivation during cytotoxic chemotherapy for cancer complicates treatment and can cause liver damage.

HBV reactivation occurs in to 10% and 50% of HBV carriers, however, risk factors are unclear.

In this study, doctors from Hong Kong assessed whether prechemotherapy HBV DNA levels influence HBV reactivation.

The optimal cut-off was at a serum HBV DNA level of  $3 \times 10^5$ .

The team evaluated 41 who underwent cytotoxic chemotherapy for breast cancer.

Of these patients, 17 developed reactivation and 24 did not.

The doctors developed a novel, ultra-sensitive, real-time PCR assay for the measurement of HBV DNA. The team measured the sera of 37 patients using this technique.

The team found that patients in the reactivation group had a significantly higher median HBV DNA load ( $1.03 \times 10^6$  copies/mL) than the nonreactivation group ( $<2.9 \times 10^3$  copies/mL).

The doctors calculated that the optimal cut-off between the 2 groups was at a serum HBV DNA level of  $3 \times 10^5$ . This gave a sensitivity of 81% and a specificity of 85%.

Dr Zhong's team concluded, "A high HBV viral load prior to the administration of cytotoxic chemotherapy is a significant predictive factor for the development of HBV reactivation".

"Such information may be useful in determining which patients would benefit most from prophylactic antiviral therapy during cytotoxic chemotherapy".

*J Viral Hepat* 2004; 11(1): 55-9

**January 28<sup>th</sup>, 2004**

## ***Health-Related Quality of Life in Patients with HIV and Hepatitis C Coinfection***

Source: [www.gastrohep.com](http://www.gastrohep.com)

Patients with HIV/HCV coinfection have similar health-related quality of life to patients with either HCV or HIV alone, find researchers in *Clinical Infectious Diseases*.

Health-related quality of life (HRQOL) is diminished in patients with both hepatitis C virus (HCV) and HIV.

However, the impact of HIV/HCV coinfection on HRQOL is unknown.

In this study, researchers from Massachusetts, USA, examined the HRQOL in patients with HIV/HCV coinfection. The team compared this HRQOL in patients with either HCV or HIV alone.

Patient groups were then compared to the United States population. Patients groups had decreased quality of life compared with the general population.

The researchers found that patients with HIV/HCV coinfection had similar HRQOL to that of patients with either HCV or HIV alone.

However, the 3 patients groups had a significantly decreased HRQOL than did the United States population.

The team found that age, unemployment, injection drug use, and depression were all associated with decreased HRQOL.

Dr Catherine Fleming's team concluded, "These findings underscore the importance of a multidisciplinary approach to the treatment of these patient populations".

*Clin Infect Dis 2004; 38: Early online publication*

### **Valeant Pharmaceuticals Advances Funding for Viramidine Clinical Trials -Company Focuses Additional R&D Investment on Viramidine**

COSTA MESA, Calif., /PRNewswire-FirstCall via COMTEX/ -- Valeant Pharmaceuticals (NYSE: VRX) today provided an update on its clinical program for the development of its antiviral compound, Viramidine(TM), a nucleoside (guanosine) analog, in oral form for the treatment of hepatitis C. In addition, the company announced that it will increase its investment in research and development to support an accelerated schedule for progressing development of Viramidine.

Robert W. O'Leary, Valeant Pharmaceuticals' Chairman and Chief Executive Officer, commented, "Our clinical data have allowed us to begin Phase 3 clinical trials for Viramidine after 12 weeks of our 72-week Phase 2 program. Our evaluation has led us to decide to further increase our total research and development expenditures in 2004 to between \$85 million and \$95 million to accelerate the clinical trials for Viramidine while continuing to support other discovery and development programs."

Valeant Pharmaceuticals has initiated the first of two global Phase 3 studies for Viramidine that will be conducted at approximately 80 sites with approximately 1,000 patients in each study. Global patient enrollment in the first study, known as VISER1 (Viramidine's Safety and Efficacy vs. Ribavirin), has commenced, and the company expects to complete enrollment in 2004.

The second Viramidine Phase 3 study, known as VISER2, is now scheduled to commence by mid-2004 with investigator meetings in the U.S., Europe and Australia. Patient enrollment in the second study is expected to begin shortly thereafter. Valeant also noted that the accelerated schedule for Viramidine may or may not accelerate the timetable for submission for approval.

The studies will compare Viramidine and ribavirin, each in conjunction with a pegylated interferon. The company has selected PEG-INTRON, a pegylated interferon marketed by Schering-Plough, for use in its first study, and has now added Pegasys, marketed by F. Hoffmann-La Roche, for use in its second study.

The Phase 3 studies are designed to treat patients for either 24 or 48 weeks, depending on viral genotypes, take patients off therapy for an additional 24 weeks, and then determine the percentage of patients with undetectable virus in their blood, as well as the incidence of anemia during the course of the entire 72-week study period.

Valeant Pharmaceuticals is continuing its Phase 2 study of Viramidine and has completed that study's 24-week treatment evaluation of safety and efficacy. Valeant intends to present the 24-week data from the Phase 2 study at the 39th Annual Meeting of the European Association for the Study of the Liver (EASL) in Berlin, Germany in April 2004, and additional data at the Digestive Disease Week (DDW) Conference in New Orleans in May 2004.

The company will host a conference call to discuss this announcement today, January 28, 2004 at 6:00 a.m. Pacific time. The dial-in number to participate live on this call is (877) 295-5743, confirmation code 5217501. International callers should dial (706) 679-0845, confirmation code 5217501. A replay will be available approximately two hours following the conclusion of the conference call through midnight on Wednesday, February 4, 2004, and can be accessed by dialing (800) 642-1687, confirmation code 5217501.

The company will also Web cast the call live over the Internet, which will be hosted in the investor relations section of its corporate Web site at [www.valeant.com](http://www.valeant.com). Participants should allow approximately five to ten minutes prior to the call's start time to visit the site and download any streaming media software needed to listen to the Internet Web cast. An online archive of the Web cast will be available following the end of the live call in the Web cast archive portion of the investor relations section at <http://www.valeant.com>.

#### *About Valeant*

*Valeant Pharmaceuticals International (NYSE: VRX) is a global, publicly traded, research-based specialty pharmaceutical company that discovers, develops, manufactures and markets a broad range of pharmaceutical products. More information about Valeant can be found at [www.valeant.com](http://www.valeant.com).*

#### **FORWARD-LOOKING STATEMENTS**

This press release contains forward-looking statements within the meaning of the federal securities laws relating to expectations, plans or prospects for Valeant Pharmaceuticals, including funding and conducting clinical trials and expected research and development expenses. These statements are based upon the current expectations and beliefs of Valeant Pharmaceuticals' management and are subject to certain risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. These risks and uncertainties include market conditions and other factors beyond Valeant Pharmaceuticals' control, the company's success in identifying

and enrolling patients in the clinical trials program, the absence of adverse events that would require the clinical trials to be prematurely terminated, clinical results that indicate continuing clinical and commercial pursuit of Viramidine is advisable, and the risk factors and other cautionary statements discussed in Valeant Pharmaceuticals' filings with the U.S. Securities and Exchange Commission.

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SourceURL: [http://www.guardian.co.uk/uk\\_news/story/0,3604,1132720,00.html](http://www.guardian.co.uk/uk_news/story/0,3604,1132720,00.html)

## **Go-Ahead for Hepatitis C Drug**

*James Meikle, health correspondent*

*The Guardian*

Thousands of patients who developed chronic liver disease after being infected with hepatitis C will be switched to more effective and expensive treatments. The decision was announced as the government steps up its battle against hepatitis C, a potential killer which has shown alarming increases over the last decade.

Official endorsement for the drug pegylated interferon, usually taken in combination with another anti-viral drug, could significantly increase the drugs bill for fighting one of Britain's most serious public health threats.

But the drug's success in treating many patients has meant that the National Institute for Clinical Excellence (Nice), the government's good-practice watchdog in England and Wales, has backed its far greater use.

Only about 2,000 patients are thought at present to use either pegylated interferon or the more standard interferon alpha, but that number is expected to grow rapidly, using regimes which could be £3,200 more expensive for each patient. Even conservative estimates put the extra cost at around £11m a year.

People infected with hepatitis C often carry it unknowingly for years. Between 50,000 and 500,000 people may have the virus. If the higher figure is accurate, far fewer than one in 10 people with the disease is diagnosed.

Around one in five known to have been exposed to the virus will eventually develop acute hepatitis, which can take more than 20 years to become evident.

Graham Foster, consultant hepatologist with Barts and the Royal London NHS trust, said: "This is the first positive step which will allow patients in the UK to receive the same treatment choice which has been available to patients in other parts of the world for many years."

## **Board OKs Free Hepatitis C Tests**

*Shanna McCord*

*Santa Cruz Sentinel*

On Tuesday, the Santa Cruz County Board of Supervisors announced that free laboratory testing will be offered to uninsured hepatitis C patients. An estimated 70 percent of the 610 hepatitis C patients treated by the county are uninsured.

With free tests available, about 30-40 additional patients can be treated annually, according to Rama Khalsa, director of the county Health Services Agency. The tests, which are part of ongoing treatment, measure enzymes in the liver and normally cost \$1,600 for each patient.

Officials estimate as many as 8,000 people in Santa Cruz County have the virus, which can go undetected for two decades while slowly eroding the liver. About 1,300 county residents know they have it.

While there is no vaccine or cure for hepatitis C, early detection allows patients the possibility of slowing the virus with medication. The virus, spread from blood-to-blood contact, most often occurs among intravenous drug users and people who received blood transfusions before 1992. It can also be contracted through body piercings and tattoos, and people who have had multiple sex partners may also face an increased risk.

The county Health Services Agency was directed to update the board of supervisors on the progress of the free tests at their meeting on March 23.

## ***Global Challenges | British Health Department Launches Hepatitis C Testing Campaign***

The British Department of Health on Wednesday announced a new campaign to encourage people to be tested for hepatitis C, APM/Reuters Health reports. A health department spokesperson said that the agency likely will publish an action plan soon, according to APM/Reuters Health. The campaign will encourage testing among high-risk groups, including injection drug users. If a person tests positive for hepatitis C, the patient would then be offered treatment and counseled about the risks of alcohol consumption, which can contribute further to liver damage caused by the disease. The plan includes a hepatitis C awareness campaign targeting the public and health care professionals. The initiative will "be centrally funded and sustained over a number of years," the spokesperson said. Officials believe that there are currently 500,000 people living with hepatitis C in the United Kingdom, but most of them do not know they are infected, according to APM/Reuters Health

*Source: APM/Reuters Health*

**January 29<sup>th</sup>, 2004**

## ***UK to Ban Chinese Herbal Remedy***

*Source: Reuters Health*

LONDON (Agence de Presse Medicale for Reuters Health) - British regulators issued proposals on Thursday to ban the Chinese herbal remedy Qian Bai Biyan Pian in the interests of public health.

The Medicines and Healthcare Products Regulatory Agency said the unlicensed product, which is sometimes used for rhinitis, could contain the Senecio plant, which can cause serious liver damage.

The agency received five reports indicating the product was still being supplied to the public, despite its call in 2002 for a voluntary market withdrawal.

## **Drug Effective For Resistant Hepatitis B**

*Will Boggs, MD*  
*Reuters Health*

NEW YORK (Reuters Health) - Chronic hepatitis B is often treated with a drug called lamivudine (brand name, Epivir) but the virus can become resistant. In this situation, an antiviral drug called adefovir, alone or in combination with ongoing lamivudine therapy, seems to be effective.

The rate of lamivudine resistance can reach 69 percent after five years of treatment, explain the authors of an article in the medical journal *Gastroenterology*. Adefovir (also called Preveon) has been shown in lab experiments to suppress lamivudine-resistant hepatitis B virus (HBV).

Dr. Marion G. Peters from the University of California, San Francisco, and colleagues assessed the safety and effectiveness of adefovir in 59 patients with lamivudine-resistant HBV.

Levels of the virus in blood specimens declined significantly in patients given adefovir alone or in combination with lamivudine, the researchers report, but not in patients receiving lamivudine alone.

Sixteen percent of patients receiving adefovir alone and 11 percent of patients receiving adefovir and lamivudine cleared the virus within 48 weeks, but none of those treated only with lamivudine did so.

Peters told Reuters Health that there appears to be no reason to continue lamivudine after beginning adefovir therapy in most cases. Combination therapy, however, should be continued in patients with cirrhosis.

**January 30<sup>th</sup>, 2004**

## **Hepatitis C Virus; FDA Approves Pegasys Prefilled Syringes**

(NewsRx.com & NewsRx.net)-- Roche announced that the U.S. Food and Drug Administration (FDA) has approved prefilled syringes of Pegasys (Peginterferon alfa-2a) for the treatment of chronic hepatitis C.

Pegasys, a pegylated alpha interferon, and Copegus (ribavirin, USP) were approved by the FDA in December 2002 for use in combination for the treatment of adults with chronic hepatitis C who have compensated liver disease and have not previously been treated with interferon alpha. Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis.

Pegasys is the most prescribed interferon therapy in the United States for the treatment of chronic hepatitis C.

Roche expects Pegasys prefilled syringes to be available in pharmacies by the end of the month. Prefilled syringes will be packaged four per box. Pegasys is currently available in vials as a premixed solution.

"Taking a medication by self-injection can be challenging for some people," said Dr. David Bernstein, director of hepatology, North Shore University Hospital. "Reducing the number of steps involved can make the process less intimidating for patients and reduce the risk of errors."

## **MISSISSIPPI: Hepatitis Investigation Ongoing at Neshoba Nursing Home**

*Associated Press*

The investigation into a hepatitis B outbreak at the Neshoba County Nursing Home could take as long as two months, according to Mississippi health officials. Since November, 16 patients at the facility have been treated for the virus. While epidemiologists are seeking to determine the cause of the outbreak, the Health Department's Office of Licensure is reviewing procedures at the nursing home, which is publicly owned but privately managed.

State health officials were notified after a patient was diagnosed with hepatitis B in November, said Lonnie Graeber, the home's administrator. That patient died; the Health Department has not determined if the death was related to the infection. After a second patient was found to be infected, all 160 residents were tested.

Under federal regulations, the nursing home was cited for a deficiency related to infection control, said Liz Sharlot, Department of Health spokesperson. The determination of a possible penalty will not be made until the investigation is completed, she said.

Board of Supervisors President James Young said board members were notified of the outbreak but had not met with nursing home officials.

*Source: CDC HIV/STD/TB Prevention News Update*