

# HCV ADVOCATE WEEKLY NEWS REVIEW

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

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Week Ending: August 2, 2008

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July 28, 2008

### ***Structure and composition of hepatitis B virus now mapped***

<http://www.news-medical.net>

Using a newly developed method, Utrecht University researchers have mapped the structure and composition of the hepatitis B virus.

The researchers were able to map the structure by spraying the virus. Their research brings us a step closer to understanding and combating hepatitis B infection. The method can also be used to analyse other viruses. The results of the search were recently published in two renowned

scientific journals: *Proceedings of the National Academy of Sciences USA* and *Angewandte Chemie International Edition* England.

To better understand and deal with viral infections, it is essential to examine the virus carefully at molecular level. However, the virus is too large to do this using the standard methods. For that reason, especially for this project, Utrecht University researcher Charlotte Uetrecht developed a modified mass spectrometer that can spray the virus intact. She did this together with Prof. Albert Heck (Utrecht University) and researchers from America and Amsterdam.

Using the modified mass spectrometer, the researchers looked at the structure and composition of the hepatitis B virus, a virus that causes severe liver ailments in humans. With the spectrometer, the researchers not only observed various forms of the virus, but they also saw the virus' molecular structure. This makes it possible in the future to block the production of viruses, and in that way to combat viral infection. The technology developed can also be used to map and identify other viruses, such as viruses that can potentially be used in weaponised form by terrorists.

Mass spectrometry is a technology with which scientists can identify molecules. Among other things, this technology is used in dope testing and for identifying paint traces in forensic investigations. Mass spectrometry works particularly well with smaller molecules. Viruses however are a million times greater in mass. To be able to use mass spectrometry nevertheless, researchers spray the virus with water through a high-tension electric charge. This technique separates the viruses from the water, enabling researchers to examine them individually. This spraying process is comparable to the transmission of a cold virus by sneezing.

<http://www.uu.nl/>

**July 29, 2008**

## ***New Drugs Provide Hope For Millions with Hepatitis C***

<http://www.thebostonchannel.com>

By Michael Lasalandra

Beth Israel Deaconess Medical Center Correspondent

Five years ago, Jacqueline Kurkowski learned as a result of a routine blood test that she was infected with hepatitis C, a potentially deadly bloodborne virus that can destroy the liver. She apparently became infected at birth.

"I couldn't believe it," said Kurkowski, now 25, who was in college when she learned she was infected. "I had never done drugs, didn't have any tattoos. And I had no symptoms other than being tired. But tests showed I was one step short of having cirrhosis of the liver. I decided to get treated right away."

Kurkowski, who lives in Stoneham and works at a drug and alcohol treatment center, received the standard treatment regimen -- 48 weeks of injections of two drugs, interferon and ribavirin. The combination of non-specific antiviral agents and immune boosters only work for up to 40 percent of patients. They didn't work for her.

"It did nothing except to make me sick every weekend for nearly a year," she said.

After the first year of treatment, she tried again, this time using a double dose. The amount of virus in her liver decreased for a while, but jumped again once she went off the double dose. When she was done, her doctors told her there was nothing else they could give her.

But Kurkowski learned of a trial of a new drug, **teleprevir**, being run at Beth Israel Deaconess Medical Center. She enrolled in April of last year. The drug, made by Vertex Pharmaceuticals, is one of two new hepatitis C treatments now in advanced clinical trials at BIDMC. The other is bocepravir, made by Schering Plough. Both drugs are known as protease inhibitors. Like the drugs used to combat the AIDS virus, they are so-called "designer" drugs that attack hepatitis C specifically. They are taken orally.

Kurkowski was skeptical, having failed two rounds of earlier treatments. "I really didn't want another negative result," she said. "I had so much hope with the other two."

But she got into the study and got her hopes up again. In the study, teleprevir was given along with interferon and ribavirin. A control group got interferon, ribavirin and a placebo. Kurkowski didn't know which group she was in. But when the study was over she learned it had worked -- she had cleared the virus from her body. A checkup six months after the study had ended confirmed the virus was gone.

"It's a great feeling," she said. "It's a huge relief. I thought I was going to have to live with this for the rest of my life, maybe get a liver transplant. I only wish the drug had been available sooner."

Dr. Nezam Afdhal, M.D., Chief of Hepatology at Beth Israel Deaconess Medical Center and Associate Professor of Medicine at Harvard Medical School, was the principal investigator for the Phase II study. He said the drug cocktail containing teleprevir cured between 62 and 65 percent of those taking it. Another study using the Schering Plough drug, **bocepravir**, in combination with interferon and ribavirin, cured 65 percent.

"These are two hot new treatments," he said. "There is new hope for patients with hepatitis C."

According to the U.S. Centers for Disease Control, about 4 million Americans are infected with the virus.

Not only do the new three-drug drug cocktails appear to be more effective than the two-drug regimen, but the addition of the protease inhibitor doesn't seem to increase the side effects to any great degree, Afdhal said. The only new significant side effect reported is a skin rash associated with teleprevir in up to 8% of patients, he said. In addition, the new cocktail appears to be able to be used for a shorter duration than the standard treatment -- 24 rather than 48 weeks, he said. Another plus is the fact that the two new protease inhibitors are designed specifically to treat hepatitis C genotype 1, which is the form of the virus most commonly found in the U.S.

Phase III trials are currently underway at BIDMC and elsewhere.

“I hope these drugs come to market soon,” said Kurkowski. “There are a lot of people out there for whom the standard treatments aren’t working.”

*Above content provided by Beth Israel Deaconess Medical Center.*

## **B.C. government failing to treat hep C epidemic: doctor**

<http://www.cbc.ca/>

Kathy Tomlinson

### *Patients denied coverage for anti-viral drugs*

A specialist who treats patients with hepatitis C is criticizing the B.C. government for denying lifesaving treatment in what he terms a full-blown epidemic.

Dr. John Farley, an epidemiologist who practises internal medicine in Vancouver and is recognized as an expert in the blood-borne infectious disease, said Pharmacare is routinely denying his patients coverage for antiviral drugs that can cure it.

"At best, I can say it is indifference to an epidemic of huge proportion," Farley said. "It is one of the most serious epidemics we are facing in our community today."

Hepatitis C is a virus that can eventually cause severe liver damage and premature death. It is spread through the transfer of bodily fluids, similar to HIV.

British Columbia has by far the highest rate of infection in Canada. An estimated 50,000 people have the disease in B.C. and the province gets approximately 300 new cases each month, according to the B.C. Centre for Disease Control (BCDC).

Although hepatitis C is often associated with drug abuse, it has spread far beyond intravenous drug users, said Farley, who has worked for the BC Centre for Disease Control, the B.C. Ministry of Health, the Canadian Society of International Health and Correctional Services Canada as an infectious disease expert.

"In my patient population about 40 per cent — maybe 50 per cent of them — who are not getting their treatment have not acquired the disease through intravenous drug use," he said. "The longer we take to treat them the more advanced it gets and the worse the outcome."

### **Denied drug coverage**

Patients who've been denied Pharmacare coverage include Teresa Iezzi, who was stuck with a contaminated needle by a troubled former foster teenager, and Michael Loring, who got hepatitis C while working as a first-aid attendant in the early 1980s.

"We didn't really protect ourselves," Loring said. "We protected the patient, which meant that I was exposed to blood and body fluids."

Loring, formerly a software support technician, now is unable to work and lives on a CPP disability pension.

"I've gotten to where — on a typical day — three to four hours is my usable day. Up until recently, maybe one or two days a week I had no energy at all," he said. "Eventually I will have permanent liver damage and I will get cirrhosis."

Anti-viral drugs such as Pegatron and Rebetron have a cure rate of between 45 per cent and 80 per cent, according to the B.C. Ministry of Health. They are approved for use in B.C., but Pharmacare won't cover the cost for patients such as Loring unless their liver enzyme levels have reached a level that indicates liver damage.

Loring said his enzyme levels are never stable, despite liver damage detected by a biopsy.

Farley said the guidelines are out of date and are contrary to what experts now know about hepatitis C.

"They [Pharmacare] don't know what they are doing because the levels can fluctuate," Farley said. "I think this is entirely unacceptable for the magnitude of the epidemic we are dealing with. Somebody does not get it."

B.C. Health Minister George Abbott said experts set the criteria for Pharmacare, and he insisted the coverage is adequate.

"I know sometimes doctors would like to immediately be able to use drugs for whatever purpose they think is right but [the guidelines] are a safeguard for patients."

### **'Epidemic' label unfair: minister**

Abbott also said he doesn't agree with Farley's assessment of the magnitude of the hepatitis C problem in B.C.

"I don't think its fair to say it's an epidemic," Abbott said. "Certainly hep C is a very big challenge — that is why we are expending about \$100 million annually in identifying preventing and treating hep C when it occurs."

Antiviral drugs cost approximately \$30,000 per patient, according to Pharmacare, depending on how the patients react to treatment.

Farley predicted if the government doesn't start covering more people the disease will continue to spread and the cost — in lives and taxpayer dollars — will be much higher.

"The average cost of hep C in B.C. is in the billions of dollars and that is from time off work, visits to the physician and hospital care when they do become ill," Farley said.

### **Huge cost predicted**

"We are now going to be facing a situation, 10 years from now probably, where our hospital beds that we need for the breast cancer patients or the other cancer patients, are taken up by liver patients. We are beginning to see that now," he said.

He estimates the cost of a liver transplant alone — the only possible treatment for end-stage liver disease — is \$100,000 or more.

"When we had the SARS [sudden acute respiratory syndrome] epidemic we spared no effort to reach and treat people. We have people who are dying [of complications from hep C] every day. Yesterday, I had two patients come in with end-stage liver disease. They came too late."

Farley said the problem is made more complicated by two of the hospitals — Vancouver General and St. Paul's — which, unlike others in B.C., refuse to accept his patients for liver biopsies because he doesn't have physician privileges at their facilities. He said it means several more months of delays for patients, who have to wait to see another specialist.

Biopsies are the only way to prove liver damage and appeal for drug coverage if the enzyme level is not at the specified level.

"That adds more cost to our health care system," he said. "And I find that abhorrent as a taxpayer. As a physician I find that it is unethical that we should not be providing the [biopsy] service."

A spokesman for Vancouver Coastal Health Authority said the policy is there to protect patients.

"There are significant complications associated with liver biopsies," Gavin Wilson wrote in an e-mail. "A process needs to be in place to ensure there is physician coverage available for these patients if and when they are admitted to hospital as a result of any complications."

Farley, who also once spearheaded a campaign to have all grade 6 students in the province vaccinated for hepatitis B, and whose groundbreaking work will be honoured by the Canadian Liver Foundation with a gala tribute in November, says he is left feeling buried under bureaucracy while his patients die.

"Where are the folks that are supposed to be responsible? What are they doing?" he asked. "Sometimes I wonder why the heck I entered medicine. I cannot give the patients what I was trained to do."

### ***Panel considers health 'standards and sanctions'***

<http://www.sfgate.com>

By KEN RITTER, Associated Press Writer

A top Nevada health official told lawmakers Tuesday that new laws could streamline oversight and responses to a public health threat such as the hepatitis C outbreak that prompted a massive patient notification effort earlier this year.

"The only way to effect change is through standards and sanctions," said state Health Division Administrator Richard Whitley.

Whitley told the Legislative Committee on Health Care that health officials in other states advised him that Nevada could enact laws requiring more public accountability and more reporting of what he called "sentinel events."

Officials should be able to issue cease-and-desist orders if they believe the public is at risk from a practice or procedure at an outpatient clinic or hospital, and health facilities should be penalized for not "self-reporting" problems, he said.

"To really restore the public confidence in the health system, having information that's public, by facility, is where we really need to go," Whitley said.

The legislative committee, chaired by Assemblywoman Sheila Leslie, D-Reno, is considering introducing a series of measures during the 2009 Legislature to revamp the reporting and handling of community health problems.

Dr. Lawrence Sands, chief health officer for the Southern Nevada Health District in Las Vegas, told the lawmakers that the hepatitis C outbreak showed "the challenge we face is balancing the right to privacy with the need to investigate crime."

The outbreak, which led to the largest public health notification operation in U.S. history, has been traced to two "source patients" treated July 25, 2007, and Sept. 21, 2007, at the Endoscopy Center of Southern Nevada, an outpatient clinic in Las Vegas.

Brian Labus, a senior Southern Nevada Health District epidemiologist, said Tuesday that records showed clinic officials had information that both patients had hepatitis C. Authorities say clinic staff members reused syringes and vials of medicine anyway, spreading the bloodborne liver disease from patient to patient.

To date, eight cases of hepatitis C have been linked to the center. A ninth case has been traced to an affiliated clinic, the Desert Shadow Endoscopy Center in Las Vegas.

The outbreak spawned state and federal criminal investigations that are continuing, and prompted health officials on Feb. 27 to begin notifying 53,000 former patients of the two clinics to get blood tests to check for hepatitis B, C and HIV, the virus that causes AIDS.

Both outpatient facilities were headed by Dr. Dipak Desai, 58, a member of the Nevada Board of Medical Examiners from 1993 to 2001, and former chairman of the board's investigative committee.

Desai's medical license has been suspended pending a hearing scheduled for early September. His lawyer told the Board of Medical Examiners on Monday that he had a stroke while he was in California last week, and was recovering at home in Nevada.

Health district officials have said 77 other people contracted hepatitis while being treated at the Endoscopy Center from March 2004 to last Jan. 11. But investigators could not conclusively link those cases to procedures at the clinic.

In all, some 400 former patients of the Endoscopy Center tested positive for hepatitis C but officials said they could not rule out that they contracted the virus through other means, including intravenous drug use, blood transfusions, organ transplants, kidney dialysis, receiving blood clotting agents before 1987, or sexual contact with a person with hepatitis C.

Sands said more than 6,000 people have enrolled in a hepatitis C exposure registry that the district established in June.

Hepatitis C results in the swelling of the liver and can cause stomach pain, fatigue and jaundice. It may eventually result in liver failure. Even when no symptoms occur, the virus can slowly damage the liver.

<http://sfgate.com/cgi-bin/article.cgi?f=/n/a/2008/07/29/state/n142806D90.DTL>

**July 30, 2008**

### ***3TC has pluses and minuses for patients with triple HIV/HBV/HCV infection***

[www.aidsmap.com](http://www.aidsmap.com)

Michael Carter

The anti-hepatitis B effect of 3TC (lamivudine) in patients with HIV appears to be greater in individuals who are also infected with hepatitis C, according to Chinese research published in the August 1st edition of the Journal of Acquired Immune Deficiency Syndromes. But the same study found that treatment with 3TC also appeared to increase replication of hepatitis C in patients infected with all three viruses.

Hepatitis B, hepatitis C and HIV can be transmitted in similar ways, and a large number of HIV-positive patients are infected with either hepatitis B, hepatitis C or both.

Since the advent of effective HIV treatment, liver disease caused by hepatitis B and hepatitis C has emerged as a leading cause of death amongst patients with HIV. But there is still little information on the impact of dual hepatitis B and C virus coinfection on the prognosis of HIV-positive patients.

Chinese investigators therefore examined hepatitis B and C replication and the risk of death in patients infected with HIV and hepatitis B and hepatitis C, and compared this to patients who were only infected with HIV and hepatitis B.

Their study included 55 patients infected with all three viruses and 73 individuals with HIV and hepatitis B. The two groups of patients were broadly similar, having average ages between 38 and 40 years.

Near equal proportions of patients in both groups were hepatitis B virus “e” antigen-positive (18% triple infection vs. 19% HIV and hepatitis B). This is an indicator of chronic infection with hepatitis B.

Of the “e” antigen-negative patients, 25% of those with triple infection had detectable hepatitis B RNA compared to 55% of patients with HIV and hepatitis B, a statistically significant difference ( $p < 0.05$ ).

After 15 months of antiretroviral treatment with a regimen that included 3TC, 6% of patients with all three infections had detectable hepatitis B RNA compared with 30% of patients infected with HIV and hepatitis B. Once again, this difference was statistically significant ( $p < 0.05$ ).

But the investigators also found that 3TC appeared to increase replication of hepatitis C. Of the triple-infected patients who were treated with this drug, 80% had detectable hepatitis C compared with 43% of triple-infected patients who received antiretroviral treatment without 3TC ( $p < 0.005$ ).

Rates of end-stage liver disease were lower amongst patients with triple infection (0.40 per 100 person years) compared to those with HIV and hepatitis B infection (0.53 per 100 person years,  $p < 0.05$ ). Furthermore mortality caused by liver disease was also lower amongst the patients with all three infections compared to those with just HIV and hepatitis B (1.22 per 100 person years vs. 2.44 per 100 person years,  $p < 0.05$ ).

Noting the different impact of 3TC therapy for patients with triple infection compared to HIV and hepatitis B infection, the investigators write that "further study is needed on the best antiretroviral regimens for patients with [HIV/hepatitis B/hepatitis C] triple infection.

### Reference

Rong-rong Y. et al. Interaction of hepatitis B and C viruses in patients infected with HIV. *J Acquir Immune Defic Syndr* 48: 491 – 92, 2008.

## ***Idenix Pharmaceuticals Advances HCV Discovery Program to Clinic***

<http://ir.idenix.com>

*~ Initiates IDX184 Phase I Clinical Study and Advances HCV Protease Inhibitor and Non-Nucleoside Polymerase Inhibitor Clinical Candidates into IND-Enabling Preclinical Studies ~*

CAMBRIDGE, Mass., July 29 /PRNewswire-FirstCall/ -- Idenix Pharmaceuticals, Inc. (Nasdaq: IDIX), a biopharmaceutical company engaged in the discovery and development of drugs for the treatment of human viral and other infectious diseases, today announced that it has initiated a first-in-man study of **IDX184** under a United States investigational new drug (IND) application. IDX184 is a once-daily, oral nucleotide prodrug polymerase inhibitor for the treatment of chronic hepatitis C. Today, Idenix also announced that it has selected a lead clinical candidate (IDX375) from its HCV non-nucleoside polymerase inhibitor discovery program and has advanced **IDX375** into IND-enabling pharmacokinetic and toxicology studies. Idenix has also advanced two protease inhibitor drug candidates (**IDX136** and **IDX316**) into IND-enabling pharmacokinetic and toxicology studies.

"We are pleased with the progress we have made in our hepatitis C discovery program in the past few months," said Jean-Pierre Sommadossi, Ph.D., chief executive officer of Idenix. "With IDX184 entering human testing and clinical candidates undergoing late-stage preclinical testing from our HCV non-nucleoside and protease inhibitor programs, we are progressing toward our ultimate goal of developing a proprietary combination of direct-acting antivirals for the treatment of hepatitis C."

### **IDX184 Nucleotide Prodrug Polymerase Inhibitor**

IDX184 is a once-daily, oral nucleotide prodrug candidate based on Idenix's proprietary liver-targeting technology that has demonstrated HCV antiviral activity in both in vitro and in vivo preclinical models. Pre-clinical testing suggests that this technology enables the delivery of high levels of active nucleoside triphosphate into the liver, the site of primary HCV infection. In HCV genotype-1 infected chimpanzees, once-daily oral administration of 10 mg/kg of IDX184 produced a mean viral load reduction of 2.3 log<sub>10</sub> after four days of dosing.

"The in vitro antiviral activity of IDX184 combined with the marked viral load reductions observed in HCV-infected chimpanzees support the potential for once-a-day, low milligram dosing of IDX184 in HCV-infected patients," said David Standing, Ph.D., executive vice president of biology for Idenix.

The company has initiated a first-in-man study of IDX184 under a U.S. IND. The study design is a double-blind, placebo-controlled, single dose-escalation study to evaluate the safety and pharmacokinetic activity of IDX184 in healthy volunteers. This study will evaluate six single rising doses of IDX184, ranging from 5 mg to 100 mg once-per-day. Each cohort of the study will evaluate eight volunteers randomized six to IDX184 and two to placebo. This study will be followed by a phase I/II proof-of-concept study in treatment/naive, HCV genotype-1 infected patients.

### **IDX375 Non-Nucleoside Polymerase Inhibitor**

Idenix has selected IDX375 as its lead clinical candidate from its HCV non-nucleoside polymerase inhibitor discovery program. Preclinical testing demonstrated that IDX375 targets the palm non-nucleoside pocket of HCV polymerase. IDX375 has exhibited single nanomolar in vitro potency against HCV genotype 1b replicon (EC<sub>50</sub> = 2 nM) and against HCV genotype 1a and 1b polymerases. Additionally, cellular cytotoxicity testing in Huh-7 cells demonstrated that IDX375 is not cytotoxic (CC<sub>50</sub> >100 micrometers), resulting in a selectivity index >33,000 for IDX375. In preclinical in vitro studies, IDX375 did not inhibit human cellular DNA polymerases alpha, beta and gamma (IC<sub>50</sub> >100 micrometers), demonstrating selectivity for the HCV 1a and 1b polymerases. After oral administration in monkeys, bioavailability of IDX375 was approximately 30%. Based on monkey plasma drug exposure levels, IDX375 has the potential for once-daily dosing in man.

### **IDX136 and IDX316 Macrocyclic Protease Inhibitors**

Idenix has scaled up manufacturing of two clinical candidates, IDX136 and IDX316, from its HCV protease inhibitor discovery program to support IND-enabling pharmacology and toxicology studies. Both IDX136 and IDX316 are based on Idenix's proprietary scaffold B and were developed through SAR (structural activity relationship) approaches aided by high-resolution co-crystal structures with the HCV protease. IDX136 and IDX316 have demonstrated single nanomolar potency against HCV genotype 1a and 1b purified proteases and nanomolar potency against HCV genotype 1b replicon (EC<sub>50</sub> = 4 to 10 nM). Additionally, these compounds are highly selective, binding tightly to the HCV protease and demonstrating no activity against eight human cellular proteases. Both drug candidates appear to have a differentiated resistance profile when compared to other macrocyclic protease inhibitors in development. Favorable pharmacokinetic properties of IDX136 and IDX316 in non-human primates suggest the potential for once- or twice-daily dosing in man.

### **Conference Call Information**

Idenix will hold a conference call and webcast today at 8:30 a.m. ET. To access the call please dial 800-471-3635 U.S./Canada or 706-758-9475 International and enter passcode 56201724 or to listen to and view the live webcast of the call, go to "Calendar of Events" in the Idenix Investor Center at [www.idenix.com](http://www.idenix.com) . A replay of the call will also be available from 11:30 a.m. ET on July 29, 2008 until 11:59 p.m. ET on August 12, 2008. To access the replay, please dial 800-642-1687 U.S./Canada or 706-645-9291 International and enter passcode 56201724. An archived webcast will also be available for two weeks after the call on the Idenix website.

### **About Idenix**

Idenix Pharmaceuticals, Inc., headquartered in Cambridge, Massachusetts, is a biopharmaceutical company engaged in the discovery and development of drugs for the treatment of human viral and other infectious diseases. Idenix's current focus is on the treatment of infections caused by hepatitis C virus and HIV. For further information about Idenix, please refer to [www.idenix.com](http://www.idenix.com) .

### **Idenix Pharmaceuticals Contact:**

Amy Sullivan: 617-995-9838

*SOURCE Idenix Pharmaceuticals, Inc.*

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

## ***Anadys Pharmaceuticals Reports Second Quarter 2008 Financial Results and Highlights***

<http://biz.yahoo.com>

SAN DIEGO, July 30 /PRNewswire-FirstCall/ -- Anadys Pharmaceuticals, Inc. (Nasdaq: ANDS - News), a clinical-stage biopharmaceutical company dedicated to improving patient care by developing novel medicines in the areas of hepatitis C and oncology, today reported its financial results and highlights for the second quarter ended June 30, 2008.

"The first half of 2008 has been a remarkably productive time at Anadys," said Steve Worland, Ph.D., President and CEO. "Through the focused efforts of our employees, we have initiated dosing in three clinical programs in six months. For hepatitis C, we commenced dosing in our Phase I clinical trial of **ANA598** during the second quarter, and are happy to announce today that we have now commenced dosing in our Phase I clinical trial of **ANA773** for HCV. We also continue to enroll patients in our ongoing clinical trial of ANA773 for oncology. We are proud of our progress to date and look forward to achieving additional clinical milestones in the coming months."

### **Financial Results**

As of June 30, 2008, the Company's cash, cash equivalents and securities available-for-sale totaled \$42.1 million.

During the second quarter of 2008 the Company had no revenue, compared to \$1.3 million for the same quarter of 2007. The revenue in the second quarter of 2007 was primarily derived from the amortization of an upfront payment and a milestone payment under a prior collaboration.

Research and development expenses were \$5.5 million for the second quarter of 2008, compared to \$7.0 million for the second quarter of 2007. The \$1.5 million decrease primarily resulted from cost savings derived from Anadys' completed strategic restructuring and associated termination of prior development programs. The decrease was partially offset by an increase in development costs for ANA773 in the second quarter of 2008.

General and administrative expenses were \$2.0 million for the second quarter of 2008, compared to \$2.3 million for the second quarter of 2007. The \$0.3 million decrease primarily resulted from cost savings derived from Anadys' completed strategic restructuring.

Operating expenses were \$7.5 million for the second quarter of 2008, compared to \$9.3 million for the second quarter of 2007. Included as a component of Anadys' operating expenses were non-cash, share-based expenses of \$0.7 million and \$1.0 million for the second quarter of 2008 and 2007, respectively.

The net loss was \$7.1 million for the second quarter of 2008, compared to a net loss of \$7.0 million for the second quarter of 2007. Basic and diluted net loss per common share was \$0.25 in the second quarter of 2008, compared to \$0.24 in the second quarter of 2007. Non-cash share-based expense resulted in a \$0.02 and \$0.04 increase in basic and diluted net loss per share for the three months ended June 30, 2008 and 2007, respectively.

During the six months ended June 30, 2008 the Company had no revenue, compared to \$2.4 million for the same period in 2007. The revenue recognized in the first six months of 2007 was primarily derived from the amortization of an upfront payment and a milestone payment under a prior collaboration. For the six months ended June 30, 2008, Anadys reported a net loss of \$14.5 million, compared to \$13.7 million for the same period last year. Basic and diluted net loss per common share was \$0.51 for the six months ended June 30, 2008, compared to \$0.48 for the same period in 2007.

### **Recent Development Program Highlights**

- **Initiation of Phase I Clinical Trial of ANA598.** In June, Anadys announced that dosing in healthy volunteers had commenced in a Phase I study of ANA598, the Company's non-nucleoside HCV polymerase inhibitor. Following completion of the healthy volunteer study, Anadys plans to transition rapidly to a short-term Phase Ib study of ANA598 in HCV-infected patients by early fourth quarter.
- **Acceleration of ANA598 Development Activities.** In late April, Anadys announced the acceleration of certain non-clinical activities for ANA598 into 2008 in order to enable a more rapid advancement into Phase II trials in 2009. The decision to accelerate the non-clinical development activities for ANA598 was based on promising results from the preclinical evaluation of ANA598.
- **Additional Mechanism in Hepatitis C Development.** In early July, Anadys announced the expansion of its development efforts in HCV to include clinical investigation of ANA773, its oral Toll-Like Receptor 7 (TLR7) agonist. As an approach to treat hepatitis C, the TLR7 mechanism is independent from, and potentially complementary to,

ANA598. Results of recently completed 13-week GLP toxicology studies have shown that with every-other-day dosing of ANA773, immune stimulation of a magnitude believed to confer therapeutic potential can be achieved without adverse toxicology findings.

- Initiation of Phase I Clinical Trial of ANA773 in HCV. Following the Company's announcement of its plans to study ANA773 in HCV, dosing in healthy volunteers has commenced in Part A of the ANA773 HCV Phase I clinical trial. The primary objectives of Part A of the study are to assess safety and tolerability. Part B of the study, which will explore every-other-day dosing over 28 days in HCV-infected patients, is expected to begin early in the fourth quarter. The primary objectives of Part B are to assess safety, tolerability and viral load decline.
- Phase I Clinical Trial of ANA773 in Oncology. Anadys continues to enroll patients in an ongoing Phase I Clinical Trial of ANA773 in oncology. The Company expects to identify a pharmacologically active dose and establish the profile of immune stimulation by year-end, which will support the design of future clinical trials of ANA773 in oncology (alone or in combination with other agents) in specific tumor types.

### **Webcast of Conference Call**

Anadys will host a conference call at 5:00 p.m. EDT today to discuss its second quarter financial results and highlights and to provide an update on its development programs. A live webcast of the call will be available online at <http://www.anadyspharma.com>. A telephone replay will also be available approximately one hour after completion of the call. To access the telephone replay, dial 888-286-8010 (domestic) or 617-801-6888 (international), passcode 79911148. The webcast and telephone replay will be available through August 13, 2008.

### **About Anadys**

Anadys Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company dedicated to improving patient care by developing novel medicines in the areas of hepatitis C and oncology. For the treatment of chronic hepatitis C, the Company is developing ANA598, a non-nucleoside polymerase inhibitor, and ANA773, an oral TLR7 agonist prodrug. The Company is also developing ANA773 for the treatment of cancer.

*Source: Anadys Pharmaceuticals, Inc.*

### **67 hepatitis B patients sue the state**

<http://www.japantimes.co.jp>

*Kyodo News*

Damages suits were filed Wednesday by 67 hepatitis B patients, or the next of kin of deceased patients, in district courts in Sapporo, Tokyo, Osaka, Hiroshima, Tottori and Fukuoka, with the plaintiffs blaming the infections on childhood vaccinations in which the same syringes were used repeatedly.

The plaintiffs are seeking a combined ¥2.5 billion in compensation from the state, which they claim was aware as long ago as 1948 that continuous use of the same syringes could lead to infection but neglected to take preventive measures.

## ***Liver damage in hepatitis C patients could be treated with warfarin, says study***

<http://www.eurekalert.org>

The drug warfarin may help prevent liver failure in thousands of people with Hepatitis C, according to new research.

In a study published tomorrow (1 August) in the *Journal of Thrombosis and Haemostasis*, researchers show that warfarin reduces the scarring on the liver caused by Hepatitis C. This scarring, or fibrosis, replaces normal liver cells and can lead to cirrhosis of the liver and ultimately liver failure.

Following the new findings in mouse models, the Imperial College London researchers are now embarking on a clinical trial of warfarin as a treatment for people with Hepatitis C, funded by the Medical Research Council (MRC).

There are an estimated 300,000 people in the UK with chronic Hepatitis C. The disease progresses much more quickly in some patients than in others and around one in five of those infected will develop cirrhosis.

Treatment to clear the infection is currently effective in only around 50 percent of patients and can have considerable unpleasant side effects such as fatigue, nausea and depression. If this treatment fails, there are no currently effective therapies to slow the progression of fibrosis.

The new research looks at how warfarin affects the progression of fibrosis in mice with chronic liver injury. Warfarin is already used to prevent and treat blood clots in people with artificial heart valves, deep vein thrombosis, and a host of other conditions.

A previous study by the same researchers demonstrated that in Hepatitis C, scarring of the liver accelerates in those patients who are prone to form blood clots. This led the researchers to believe that warfarin's anti-clotting properties might enable the drug to fight the disease.

The new study showed that treatment with warfarin significantly reduces the progression of fibrosis in normal mice with chronic liver injury. It also shows that warfarin reduces the progression of fibrosis in mice with chronic liver injury and a genetic mutation known as Factor V Leiden (FVL), which causes fibrosis to progress at a much faster rate than usual because it amplifies the body's clotting mechanisms.

Professor Mark Thursz, one of the authors of the study from the Division of Medicine at Imperial College London, said: "At the moment there are a great many people with Hepatitis C who have no treatment options left and it would transform their lives if we could prevent them from developing liver failure. We are looking forward to seeing the results of our upcoming trial in humans now that we've had such promising results in the trial in mice."

Dr Quentin Anstee, an MRC Clinical Research Fellow and the corresponding author of the study from Imperial College London, added: "If we have positive results from the new trial, we will have a potential treatment that is already available and very cheap, and which should be safe

enough for people to take. If we are successful in Hepatitis C patients, we are hopeful that such treatment might benefit people with liver damage from other causes, and this is something we would be keen to study further."

The researchers are recruiting 90 patients for the new trial who have undergone a liver transplant as a result of liver failure caused by hepatitis C. A third of such patients progress very rapidly to fibrosis following transplantation.

The researchers hope that treating these patients with warfarin will prevent this liver damage and improve their prognosis. Transplant patients have a liver biopsy every year following transplantation to assess their progress, and the researchers will analyse data from this biopsy to establish the effectiveness of the warfarin treatment. The two-year trial will take place across five centres including Imperial College Healthcare NHS Trust, which has integrated with Imperial College London to form the UK's first Academic Health Science Centre.

The trial is taking place in transplant patients because the researchers estimate that it would take 10-15 years to conduct a trial in patients in whom the disease was progressing at a normal rate.

### ***New treatment therapy helps inhibit hepatitis C***

<http://www.physorg.com>

Two new studies examine the use of the nucleoside polymerase inhibitor, **R1626**, to the standard therapy for hepatitis C. The reports appear in the August issue of *Hepatology*, a journal published by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases (AASLD).

The first study shows that adding the treatment to standard therapy with pegylated interferon alpha plus ribavirin leads to a synergistic antiviral effect. In the search for new and better treatments, researchers have been testing R1626, which previously has been used to inhibit HCV replication in vitro.

The study group included 104 patients with HCV genotype 1. Twenty-one took 1500 mg of R1626 twice a day along with peginterferon alpha-2a. Thirty-two took 3000 mg of R1626 twice a day along with peginterferon alpha-2a. Thirty-one took 1500 mg of R1626 twice a day along with peginterferon alpha-2a and ribavirin. And 20 took the standard of care treatment of peginterferon alpha-2a with ribavirin.

After four weeks, HCV RNA was undetectable in 29 percent, 69 percent, and 74 percent of patients in the respective study arms, compared to 5 percent of patients receiving the standard of care treatment.

"The results of the present study show a marked increase in antiviral effect in patients when ribavirin is added to the combination of R1626 and peginterferon alfa-2a," the authors report.

In conclusion, the authors report, "this phase 2a study has demonstrated a potent reduction in HCV RNA by R1626 and high viral responses with up to 74 percent rapid viral response after 4 weeks of treatment. The strong antiviral effect between R1626, peginterferon alfa-2a and

ribavirin, suggests that the dose of one or both of these agents could be lowered to improve tolerability without significantly compromising efficacy."

A second study shows that, in patients with chronic hepatitis C, the antiviral activity increased with the dosage. Side effects were tolerable and there was no evidence of viral resistance.

For 14 days, the patients were treated with R1626 orally at twice-daily doses of either 500 mg, 1500 mg, 3000 mg, 4500 mg, or placebo. "The decreases in HCV RNA from baseline observed with R1626 indicates potent antiviral activity and lack of viral load rebound in the significant majority of patients following 14 days of monotherapy," the authors report. Current therapy for patients with chronic hepatitis C virus (HCV) requires up to 48 weeks of treatment.

In addition, the study showed that R1626 was well tolerated up to 3000 mg and there was no evidence of viral resistance in this study, perhaps reflecting the potency of R1626 as an anti-viral agent.

*Source: Wiley*

**August 1, 2008**

### ***Free HIV, Hepatitis C testing available – Spencer, Iowa***

<http://www.spencerdailyreporter.com>

Free HIV and Hepatitis C testing will be available in Spencer from 10 a.m.-2 p.m. on **Friday, Aug. 8** at the Spencer medical Arts Building, 116 E. 11th St., Suite 206.

"The HIV and Hepatitis C testing provided in Spencer by Siouxland Community Health professionals is free and confidential," said Colette Rossiter, RN with Spencer Hospital Community Health and Clay County Public Health. Appointments are not necessary. Those interested in being tested should use the north entrance of the Spencer Medical Arts Building and take the stairs or elevator to Suite 206 on the second floor.

According to the Center for Disease Control and Prevention (CDC), there are over 1 million HIV-positive individuals in the United States. One-fourth of them don't know they're infected, and may be unknowingly spreading the virus. The first step is to know one's status.

"Testing is the only way to know if you are infected with HIV, the virus that causes AIDS. We would like to test those who have a history of high risk behaviors, such as unprotected sex and needle sharing," Rossiter explained. "In addition, Hepatitis C testing is available for anyone who has received a blood transfusion or organ transplant prior to July 1992; has been on long-term hemodialysis; or has used or shared needles for injection of street drugs or steroids."

This free and confidential testing is being sponsored by Siouxland Community Health, Spencer Hospital Community Health Services, and Clay County Public Health. For more information call Clay County Public Health at 264-6468.

## **Low hep B vaccination rates seen in newborns**

[www.reuters.com](http://www.reuters.com)

NEW YORK (Reuters Health) - The results of a survey conducted by the US Centers for Disease Control and Prevention indicate that only about 50 percent of newborns receive a dose of hepatitis B vaccine before hospital discharge.

In 1991, the Advisory Committee on Immunization Practices recommended that all newborns receive the first dose of the vaccine before leaving the hospital or at age 1 to 2 months. In 2002, however, this recommendation was changed to indicate a preference for vaccination prior to hospital discharge. Finally, in 2005, the guidelines were again revised to recommend pre-hospital discharge hepatitis B vaccination for all medically stable infants weighing at least 2000 grams (4 pounds 6.5 ounces).

The present findings are based on an analysis of survey data obtained after the 2002 guidelines were implemented but before the 2005 ones were in place.

Overall, 43 percent of newborns received the first dose of the hepatitis B vaccine by age 1 day and 50 percent had received it by age 3 days, CDC researchers report in Friday's *Morbidity and Mortality Weekly Report*, publication of the CDC.

Wide variations in vaccine coverage were seen between cities and states. Detroit, Michigan had the highest coverage at 77.5 percent, while Fresno County, California had the lowest at about 8 percent.

Infants infected with the hepatitis B virus have a 90 percent chance of becoming chronically infected, which can lead to cirrhosis and liver cancer, CDC researchers note.

Delivery hospitals play a key role in the national strategy to prevent hepatitis B transmission and should have policies and procedures in place to ensure that hepatitis B vaccination is administered to all newborns before they leave the hospital, they emphasize.

*SOURCE: Morbidity and Mortality Weekly Report, August 1, 2008.*

## **Vertex hepatitis C drug meets study goal**

<http://biz.yahoo.com>

CAMBRIDGE, Mass. (AP) -- Vertex Pharmaceuticals Inc. said late Thursday its hepatitis C drug candidate telaprevir was both safe and prompted a response in patients during a midstage study. Interim results from a Phase IIa clinical trial showed that twice-daily and three-times-daily doses of telaprevir in combination with standard hepatitis C treatments were effective in prompting a response. More than 80 percent of 160 patients had undetectable levels of hepatitis C after four-week and 12-week periods.

A complete analysis will be performed upon the conclusion of this study in 2009, the company said.

## **Frequent HCV Exposure Tied to Immune Responses**

[www.reuters.com](http://www.reuters.com)

NEW YORK (Reuters Health) Aug 01 - Injection drug users who successfully clear HCV infection have a reduced risk of re-infection. Now, in long-term injection drug users frequently exposed to the hepatitis C virus (HCV), analysis of virus-specific immune responses has shown that resistance to re-infection is correlated with T cell responses.

Dr. Barbara Rehermann of the National Institutes of Health in Bethesda, Maryland and colleagues studied 66 individuals with long histories of injecting illicit drugs. They report their findings in the July 15th issue of the *Journal of Infectious Diseases*.

HCV-specific T cell proliferation and interferon gamma production were present in 94% of subjects who were enzyme immunoassay positive but non-viremic. This was true of only 45% of their viremic counterparts and 62% of the negative non-viremic subjects.

In addition, 90% of viremic subjects had neutralizing antibodies, compared to 56% of those who were positive but non-viremic, and none who were negative and non-viremic.

The widespread presence of antibodies in the non-viremic subjects is contrary to findings in other studies, say the investigators, and is most likely due to frequent HCV re-exposure because of continuing injection drug use.

Given that the reduced risk for HCV persistence in drug users with previous infection was correlated with T cell responses, the investigators conclude that "prolonged antigenic stimulation appears to be required to maintain humoral responses."

*J Infect Dis* 2008;198:203-212.