

# HCV ADVOCATE WEEKLY NEWS REVIEW

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

*Alan Franciscus  
Editor-in-Chief*

Week Ending: April 26<sup>th</sup> 2008

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April 19<sup>th</sup>, 2007

## ***Task force fights drug use and its effects in two counties***

<http://www.theprogressnews.com>

By Josh Woods Staff Writer

DUBOIS - Clearfield-Jefferson Heroin Task Force has elected voting board members for terms ending in March and reorganized the format of its monthly meetings.

Sandy Township Police Chief Don Rouch was selected the task force's new chairman, while Bev Kurts will serve as vice chairwoman.

Angela Ireland, Jeff Pisarcik, Fran Rosana and Mary Lash were appointed to the voting board.

Task force coordinator Susan Ford discussed the group's annual plan, suggesting the change in meeting format. Mrs. Ford said that she favored allotting time to break into committees at every other meeting, so that the group could accomplish things it has not been able to do due to time constraints. A vote to change the meeting format was approved unanimously.

Mrs. Ford suggested the committees take a look at the force's school programs, as well as the hepatitis C program. A committee may also be formed to look into a "reality tour" program.

"The reality tour program was developed by Norma Norris of Candle Inc.," said Mrs. Ford. "Basically it is a walk-through of a heroin user's life.

"The program features real-life, volunteer actors who act out a hospital scene, a jail scene, a morgue scene. ... The idea is to give the community awareness of what can happen."

The force also heard an update on the hepatitis program. From May 1, 2007, to March 1, 2008, 77 people were screened through the program for hepatitis C. Of the 77, 45 were identified as substance abusers and 32 as other risk factors. The number of positive screens was 24, which Mrs. Ford noted was a higher percentage (31 percent) than a recently reviewed screening in Philadelphia.

Of the 24, only half followed up with a PCR test. Other findings show that only six people identified as substance abusers followed through with Intensive Case Management Services.

"We need to increase the number of people that follow up with a PCR test and with Intensive Case Management," said Mrs. Ford. "We need to find a way to change perception."

Clearfield-Jefferson Heroin Task Force initiated the hepatitis C program in 2004 after Dr. Tuesdae Stainbrook noticed a dramatic increase in heroin use and hepatitis C cases in the

Clearfield-Jefferson county area.

The force received a grant through the Department of Health's Bureau of Drug and Alcohol program for the screenings.

Voting board member Ruthanne Barbazzeni announced that a free, parents-only community awareness night will be held on April 28 from 7-8:30 p.m. at the Clearfield Area Middle School auditorium.

Elaine Surma of the attorney general's office will provide parents with information on how to protect their children from current drug trends.

"Right now we're looking to restructure the task force and make it more accessible to the community," said Mrs. Ford. "Currently we are holding meetings in DuBois because it is a halfway point between the two counties.

"We would ask that anyone who is interested come out to the meetings. We're not asking anyone to commit all of their time. We just want individuals who have a desire and can give us a few new ideas. It's a chance for people to be a part of something good in their community."

The next meeting of Clearfield-Jefferson Heroin Task Force will be held on May 15 at noon at the DuBois Area Middle School.

## ***HCV Drug Could Be A Winner***

<http://money.cnn.com>

When you're close to the finish line and the competition is lagging way back, it's tempting to ease up. Not so at Vertex.

In the race to get a better hepatitis C drug to patients, Vertex (VRTX) wants to be the standard of care before competitors show up.

Hepatitis C, or HCV, can lead to liver disease and cancer. It has infected 170 million people worldwide -- more than five times the number with HIV/AIDS.

By 2010, the market for HCV treatments will be \$4 billion, says analyst Brian McCarthy of Merriman Curhan Ford, which seeks Vertex's business. He sees the market rising to \$8 billion by 2015.

Kurt Graves, Vertex's chief commercial officer, figures there might be 4 million people with HCV in the U.S, with 2.5 million undiagnosed or untreated .

Vertex's drug, a protease inhibitor called Telaprevir, has started phase three clinical trials and could reach the market by 2011.

"I see no reason to doubt Vertex's ability to get to market first," McCarthy said. "And Telaprevir could potentially alter the standard of HCV care."

On April 24 Vertex will outline details about Telaprevir's effectiveness at a European conference.

Those details no doubt will interest rival HCV drug developers like Schering-Plough (SGP), Roche (RHHBY), AstraZeneca (AZN), Pfizer (PFE), Pharmasset (VRUS), InterMune (ITMN), Anadys (ANDS), Idera (IDRA), ViroPharma (VPHM) and Idenix (IDIX). Some of their drugs are in phase two trials.

"Competing drugs will enter the picture just as Telaprevir hits peak sales," McCarthy said.

#### THE FINANCIALS

Vertex shares, which trade near 26, have surged more than 80% since March 18.

The big bump came on March 31, when shares rose 28% after the company cited data from a midstage study showing hepatitis C patients responded to Telaprevir. But the stock still remains well off its 52-week high of 41.42, set in September.

Thomson Reuters analysts see losses edging down to \$2.93 a share this year from \$3.03 in 2007. Losses are expected to narrow to \$2.83 in 2009, with the first profit, at \$2.16 a share, projected for 2012.

The company has one drug on the market, shared with Glaxo, but gets most of its revenue from partners with deep pockets.

#### THE COMPANY

Partnerships are a key part of Vertex's strategy to develop Telaprevir. The company has deals with the Janssen unit of Johnson & Johnson (JNJ) unit and with Mitsubishi Pharma.

Vertex will share North American sales with Janssen and get 20% of Janssen sales in Europe, South America, the Middle East, Africa and Australia. Mitsubishi will market in Japan and other Asian countries.

Janssen has paid Vertex \$165 million upfront and \$30 million of a potential \$380 million in milestones. The Mitsubishi deal is for \$33 million plus royalties.

#### LOOKING AHEAD

Vertex has second-generation protease inhibitors in the works on which it plans to build a multidrug portfolio around Telaprevir, Graves says.

"We're looking at technology to license in that could complement Telaprevir," he said.

### ***Hep C Forum Draws Big Crowd***

<http://www.lasvegasnow.com>

Patients caught in the middle of the hepatitis C scare showed up in force to a Saturday forum hoping to get some answers.

More than 200 people listened to a panel comprised of health officials, lawyers and even mental health providers. The forum was put together by the Southern Nevada Health District.

"It let me get a lot of anger out of me," said Jayne Svela who says her anger has been building since learning she was infected with hepatitis C. Even though Svela called the forum a good opportunity to vent, she didn't feel she got real answers.

"They are trying to make us feel good about having hepatitis C and there not saying who is responsible and they are not saying what they are going to do to go after the people that did this to us."

Tables were set up offering information, mostly health information on the disease.

"Some of the symptoms I have now I can attribute to hepatitis C that I didn't know before, so now it makes me more aware so that when I go see my doctor I can say now I know why I'm having this," said James Romero, tested positive for hepatitis C.

Representatives from drug companies were on hand to explain what treatments are available and how hepatitis C can be managed.

"Seeing them walk away with a look of a little bit of relief, you gave them a little bit of information that they can go home and feel wow this is not a death sentence," said Bob Bravin, helping inform patients about hepatitis C.

But beyond the pamphlets many say the forum gave them very little.

"These people are talking about the grief that we are going to go through but no one wants to discuss who is responsible for this and what is happening to the people responsible for this," Svela said.

The health district says the goal of the forum was to link people to resources. Unfortunately they couldn't answer many questions about the investigation in to the endoscopy clinics or what will happen to the doctors and staff of those clinics.

"Definitely got some knowledge in terms of what some of the concerns are in the community what some of the deficits are in terms of things that we could be doing better or expand on," said Dr. Lawrence Sands, Southern Nevada Health District.

Right now only the Endoscopy Center of Southern Nevada is being linked to the hepatitis infections. They're being investigated for reusing syringes and vials of medicine. More than 40,000 people in Clark County have been notified that they may have been exposed to the disease.

One question that remains unclear is when patients will get their medical records back from Metro.

Attorneys representing patients who have filed lawsuits against the doctors met on Friday as they prepare for a class action lawsuit.

"I have 225 infected patients. I've been able to get the records for one client from Metro, and I think everyone is having the same type of difficulty," said attorney, Robert Eglet.

The health district has indicated that Metro is hiring a third party to handle the records.

The legislative committee on health care will meet Monday at 9 a.m. at the Grant Sawyer building. Lawmakers are expected to get a full update on the hepatitis investigation. Las Vegas ONE, Channel 19 and LasVegasNOW.com will have live coverage.

**April 21<sup>st</sup>, 2007**

## ***Tennessee health officials investigate acute hepatitis B outbreak in Hawkins County***

<http://www.timesnews.net/>

Officials with the Northeast Tennessee Regional Health Office said Monday they have investigated eight cases of acute hepatitis B in Hawkins County since the beginning of the year. Seven of the cases were residents of Hawkins County and one was a resident of Hancock County.

"These numbers reflect a significant increase in reported cases as compared to previous years. Only four cases were reported in Hawkins County in each of the past two years," said Dr. Lawrence Moffatt, regional medical director. "In response to this situation, the Hawkins County Health Department is increasing its efforts to identify additional cases and is offering vaccine to at-risk close contacts of identified cases."

Hepatitis B is a serious disease caused by a virus that attacks the liver. In about one in 20 infected adults, the virus can cause life long infection, which can lead to cirrhosis of the liver or liver cancer.

According to the health department, hepatitis B has a very slow onset of symptoms. Those symptoms include loss of appetite, abdominal pain, nausea and vomiting and jaundice. Some infected persons may show no symptoms at all. Symptoms usually occur two to three months after exposure, but can occur up to six months after exposure.

Hepatitis B is spread through contact with blood or body fluids that contain blood. It can be spread through unprotected sexual contact with an infected person, sharing needles or anything that breaks the skin that has been contaminated with the blood of an infected person, such as tattooing or ear piercing equipment. It can also be spread from mother to infant, unless the infant is vaccinated to prevent it.

Hepatitis B can be prevented by avoiding high risk activities and by immunization with the hepatitis B vaccine. It is routinely given to all infants and children as well as adults who have not been vaccinated and are at risk. It is routinely given to all infants and children as well as adults who have not been vaccinated and are at risk.

Health department officials said if you believe you may have hepatitis B, please contact your healthcare provider or the local health department. If you believe you may be at risk for hepatitis

B and want to find out if you need the hepatitis B vaccine call your local health department or the Regional Health office at 423-979-3200.

## **8 Reported Cases Of Hepatitis C**

<http://www.ktnv.com>

The Southern Nevada Health District has identified an additional case of acute Hepatitis C in a patient who underwent a procedure at the Endoscopy Center of Southern Nevada, 700 Shadow Lane.

This additional case brings the total number of acute Hepatitis C cases associated with this outbreak to eight, and it is the seventh linked directly to the clinic.

The eighth case underwent a procedure at the clinic in June 2005 and developed symptoms of acute Hepatitis C nine weeks after the procedure.

The patient had no other reported risk factors for the illness and has since recovered.

*The health district's investigation is ongoing and it continues to receive more than 150 reports of positive Hepatitis C cases daily.*

*Typically, the health district receives 20 to 40 positive reports daily.*

The higher numbers are expected based on increased rates of testing and the background rate of the disease.

Interviews of patients of the Endoscopy Center of Southern Nevada who have tested positive for Hepatitis C have begun.

Patients who had procedures requiring injected anesthesia at the center in January will have to wait six months from their procedure date to be tested and therefore the interview process will take several months to complete.

The Southern Nevada Health District continues to update information on its web site, including patient and physician information at <http://www.southernnevadahealthdistrict.org/>.

In addition, the health district has set up a hotline at 702-759-4636 (INFO).

**April 22<sup>nd</sup>, 2007**

## **Legacies of endurance**

<http://www.boston.com>

By Adrian Walker  
Globe Columnist

There's a song by The Calling with lyrics that stuck in Laura Dempsey's mind yesterday. The song is called "Our Lives" and it includes the following verse:



*Cause these are the  
days worth living  
These are the years we're given  
And these are the moments  
These are the times  
Let's make the best  
out of our lives*

Actually, the song wasn't just in her mind: the last line was written on the singlet she wore as she ran the Boston Marathon in memory of her late friend, Laura Linehan.

Dempsey has run the race the last three years to honor her friend, and to raise money for the American Liver Foundation; yesterday, she ran it in her friend's memory. Linehan, of Melrose, died during liver transplant surgery earlier this month.

"I had her in my mind the whole time," Dempsey, of Watertown, said after the race, which she finished in a little over four hours. "In some ways it was very motivating, and in other ways it was sad. I was very heartbroken that she wasn't going to be here physically. I just put one foot in front of the other. She was with me every step of the way."

Linehan died at the Mayo Clinic in Jacksonville, Fla., after battling liver disease for much of her life. She contracted liver disease as an infant. During transplant surgery when she was 2, she received a blood transfusion that resulted in her contracting Hepatitis C.

Her final days could not have been more wrenching. She was near death when her parents made a televised appeal for a liver. A donor liver was located at 5 a.m. the next morning - the miracle her family and many friends had been hoping for. But a few hours later, unable to withstand the surgery, she was gone. She was 20 years old.

Unlike most people of any age, though, Linehan left a legacy. She and her family became actively - urgently - involved in persuading the public to become organ donors, and her life has helped raise awareness about liver disease.

Ann Linehan, Laura's mother, was at her daughter's side for every gut-wrenching second of her ordeal. Yesterday she was on the course, in Coolidge Corner, cheering Dempsey on.

"I'm still trying to recover from three things," she said. "One, her death itself; two, the horrible 18 days she spent in (intensive care) before she died; and three, the past 19 years of living with liver disease. Now, it's all gone."

Her daughter's death has left her with a purpose. "I'm determined to have her life make a difference," Linehan said. "Although she can't continue on, our family will, and we want to raise awareness and find a cure for hepatitis."

Linehan went to a brunch at the Westin Copley Place Sunday saluting some of the runners. The team running for liver research - some 248 strong - was honored, and there were tributes to Laura Linehan.

"Laura would have been thrilled," Linehan said. "She and Laura were so close, and supporting her in her run was something Laura always wanted to do."

The Lauras, Dempsey and Linehan, got to know each other a few years ago, when Dempsey was preparing for her first marathon run. They formed an instant bond, one that has changed Dempsey's life. She worked in sales at the time, unhappily. Now she works as a fund-raiser for the American Liver Foundation.

"I learned a lot about liver disease during my first run," said Dempsey, 32. She raised \$11,000 yesterday for research. "Everything in my life changed after getting to know Laura and to know about the ALF."

That song Dempsey quoted on her back had been played at Laura Linehan's graveside. The song is not about death, which is precisely why it reminds her of her late friend.

"It's not about dying, it's about living, and how we have to make the most of our lives," Dempsey said. "That's exactly what she did in her short time."

*Adrian Walker is a Globe columnist. He can be reached at [walker@globe.com](mailto:walker@globe.com).*

### ***Saint Louis University Liver Center receives \$200,000 gift***

<http://www.bizjournals.com>

Friends of the Saint Louis University Liver Center donated \$200,000 to the center to help fund research into treatments for liver disease, as well as help fund operating costs, including for faculty and staff salaries, visiting professorships and patient-oriented seminars.

The Friends organization has raised and donated more than \$1.6 million to the Liver Center since 2003, the year after the group was formed by a group of patients.

The Saint Louis University Liver Center treats more than two dozen types of liver disease, of which hepatitis C is one of the most common, affecting some five million Americans and their families.

Established in 1836, Saint Louis University School of Medicine has the distinction of awarding the first medical degree west of the Mississippi River.

[matthewallen@bizjournals.com](mailto:matthewallen@bizjournals.com)

### ***Technology To Detect Liver Disease Via Blood Test To Be Developed***

<http://www.medicalnewstoday.com>

No simple blood test exists to determine which of the millions of people infected with hepatitis C virus will develop cirrhosis of the liver or cancer. Now, researchers are developing new technology to find blood proteins that herald the earliest signs of chronic liver disease. If successful, they hope to extend the use of the technology, and to do the same for many other

diseases and to make it commercially available for broad clinical use.

Washington State's Life Sciences Discovery Fund Board of Trustees has announced that the collaboration between scientists at the Department of Energy's Pacific Northwest National Laboratory and the University of Washington Liver Transplantation Program in Seattle will receive \$4.8 million over the next three years to develop a new proteomics technology and apply it in search of biomarkers for liver disease.

"This is really fantastic," says grant recipient and lead investigator Dick Smith of PNNL. "This funding will support work that is almost impossible to get funded by conventional sources. The grant brings together a larger program that could have significant positive impacts on the health of people, certainly in Washington, but in the whole country as well."

The announcement caps a lengthy selection process by LSDF. "This has been a highly-competitive process. The proposals were weighed on their scientific merits and their abilities to utilize this funding to provide statewide economic returns, to build a competitive life sciences industry and to advance the health of, and health care for, our citizens. These newly-awarded grants will leverage substantial additional investment in Washington State by a variety of other funders such as federal agencies and philanthropic organizations," says LSDF Executive Director Lee Huntsman.

About 1.6 percent of the U.S. population has signs indicating they have been or are infected with hepatitis C virus, and up to 12,000 people each year die from HCV-induced liver damage and cancer. A percentage of infected people develop various levels of liver disease -- the worst requiring liver transplants -- but doctors have no way of telling who's most at risk.

PNNL's Smith is leading development of the new technology at DOE's Environmental Molecular Sciences Laboratory on the PNNL campus. In collaboration with UW's Michael Katze, Smith's group will use proteomics to compare blood and tissue samples from individuals who have advanced liver disease or are healthy to find proteins that indicate the potential for advanced illness.

The researchers' long term goal is to make such technology efficient and inexpensive enough for use in clinical settings. In addition, Smith's development plans include making the technology widely applicable to biomarker searches for other diseases.

*Article adapted by Medical News Today from original press release.*

### **10% of people given fibrinogen have HCV**

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

*The Yomiuri Shimbun*

About 10 percent of the 7,400 or so patients who were administered the blood product fibrinogen were infected with hepatitis C, a Health, Labor and Welfare Ministry study team announced Tuesday.

The team has been investigating patient records kept at medical institutions to which fibrinogen

was shipped. The product was made by Green Cross Corp., a predecessor of Mitsubishi Tanabe Pharma Corp.

An estimated 10,000 people are thought to have been infected with the hepatitis C virus after the blood product fibrinogen was used in surgical operations involving about 280,000 people. However, the results of the investigation suggest this percentage of infection, 3.6 percent, could be lower than the true figure, medical sources said.

In its interim report, the study team found 99 people infected after being treated with fibrinogen have died from hepatitis-related diseases.

Fibrin glue, used as a surgical adhesive, was the most common use of fibrinogen among patients, making up about 40 percent of cases. Direct intravenous injection of fibrinogen as a hemostat agent in operations, including parturitions, accounted for 30 percent of treatments involving the product.

The survey results prompted the ministry to renew its call for people who have had surgery to have hepatitis checkups.

Out of 6,609 medical institutions to which Green Cross delivered the product, 644 institutions that kept individual patients' records of administration of fibrinogen were surveyed at the end of February. Of them, 475 institutions provided valid responses.

According to the survey, 7,406 patients were administered fibrinogen, and 741 of them were found to have been infected with HCV. Of them, 12 also had been infected with the hepatitis B virus, while 40 others had been infected with HBV alone.

Hospitals are unsure whether 4,908 of the 7,406 patients have hepatitis. The number of people found to have been infected likely will further rise as the investigation progresses, the medical sources said.

Of patients administered fibrinogen, 1,817, or 24.5 percent, have already died. Of them, 99 died from hepatitis-related diseases.

**April 23<sup>rd</sup>, 2007**

### ***Biotech Wins Right to Load Magic Bullet***

<http://www.therapeuticsdaily.com>

*Herald Sun* (Australia)

IT IS not often that a small Melbourne biotechnology company scores a victory in the US Supreme Court.

That's what has happened to Benitec, which has been tied up in complex US litigation with Nucleonics since 2004.

It has been a long road for the company that has been tenaciously clinging to its intellectual property in the face of better funded litigants.

According to one source, Benitec would not have survived this long without litigation insurance.

However, now that the Supreme Court has refused Nucleonic's appeal, Benitec can concentrate on science rather than law.

CEO Sue MacLeman described it as "fantastic news" and Benitec's gene silencing technology is also attracting external admirers.

Benitec shares rose sharply in January when the company signed a deal with the world's biggest pharmaceutical company, Pfizer, to develop and commercialise its Hepatitis C virus compound.

The appointment of experienced researcher Dr Jason Smythe as chief scientific officer last year also bolstered confidence in the stock.

In laymans terms, Benitec has a platform technology known as vector expressed RNAi which holds the promise of one day managing and in effect curing many human diseases. In the same way that many vaccines often use a denatured virus to promote the immune system, Benitec's technology uses a harmless virus (vector) to carry the RNAi molecules to the diseased cells.

The diseased cell then starts to make its own medicine -- an effect that can theoretically last for months, years or even a lifetime.

Benitec's lead drug is undergoing trials in California's City of Hope and aiming to promote resistance to the HIV-1 virus in AIDs patients with lymphoma. Other potential targets include Hepatitis B, Huntington's disease and some cancers.

Benitec shares closed up 0.5 or 5.26 per cent to 10.

## ***Liver Diseases: A Huge European Health Burden, But Some Trends Are Positive***

<http://www.prnewswire.co.uk>

- *29 Million EU Citizens (6%) Have Liver Diseases, 5th Most Common Cause of Death*
- *Yearly, Liver Cancer Alone Takes 40,000 Lives; Alcohol Abuse Takes 13,000*
- *Number With Fatty Liver Disease Stable or Growing; Viral Hepatitis Declines*

More than 6,000 physicians and scientists from around the world gathered today in this historic Italian city to attend the opening sessions of the 43rd Annual Meeting of the European Association for the Study of the Liver (EASL), which runs until April 27th. Not surprisingly, several of the first presentations focused on trends in the prevalence of each of the major liver diseases, including continuing declines in new cases of hepatitis B and C, but stability or increases in fatty liver disease due either to excessive consumption of alcohol or non-alcoholic causes (NAFLD - non-alcoholic fatty liver disease).

Hepatologists (liver disease specialists) study and treat a variety of acute and chronic conditions affecting this largest internal organ of the body. The acute category includes diseases that typically result from inflammation or infection due to injurious agents such as viruses, alcohol,

and drugs. The most prominent conditions - each of which may arise in an acute form but then progress to a chronic state -- are alcoholic liver disease; hepatitis B, C, and D; non-alcoholic fatty liver disease (NAFLD); and NASH (non-alcoholic steatohepatitis, the most severe subset of NAFLD).

The transition from an acute to a chronic state occurs when the patient fails to recover and the acute infection or disease produces ongoing damage to the liver. Cirrhosis - which refers to the death of liver cells, altered cell regeneration, deposition of fibrous scar tissue, and ultimately the impairment of liver function - represents the final stage of many chronic liver diseases. Cirrhosis can only partially be reversed, but treatments can stop or slow its progression. When uncontrollable complications of cirrhosis occur, or when damage precludes sufficient liver function, a liver transplant becomes necessary. Cirrhosis is the major risk factor for the development of hepatocellular carcinoma (HCC), a primary cancer of liver cells, which may also require transplantation.

Estimates suggest 10 million carriers of viral hepatitis in Europe, of which over 8 million are infected with HCV. Although statistics vary widely by country, HCV accounts for a large (or in some countries, majority) proportion of all cases of cirrhosis and HCC. Although precise figures are not available, alcoholic liver disease is a growing problem in both Western and Eastern Europe, in part because of changing lifestyles and the increasing numbers of women and adolescents who drink to excess (a problem that in the past was largely a phenomenon of adult males). The Dionysos study, conducted in Northern Italy, reported that 4% of the population had alcoholic liver disease of varying severity. Alcoholic liver disease is the second most common indication for liver transplantation, after HCV. NAFLD and NASH denote fatty infiltration of the liver that are not due to excessive alcohol, and are related instead to insulin resistance, type 2 diabetes, obesity, and the metabolic syndrome. These abnormalities are now receiving considerable attention not only because they may progress to liver cirrhosis, but also as additional risk factors for cardiovascular disease. The best current estimates suggest that in the general population NAFLD can be found in 3% to 24% of adults.

Despite improved prevention, diagnosis, and treatment, the overall costs of liver disease remain very high because of an increase prevalence of selected conditions, and the common progression to a chronic state possibly leading to life-threatening complications.

### **About EASL**

The European Association for the Study of the Liver (EASL) aims to promote investigation into liver disease and improve the treatments that currently exist for these conditions. The association, through its annual meetings, seeks to inform and educate both the scientific community as well as society in general about the increasing occurrence of liver diseases along with the importance of understanding these conditions in order to treat and prevent them. Since its creation in 1966, the EASL congress has been hosted in 20 different European countries. Currently the association has over 1400 members and the annual congress attracts over 6000 delegates from over 65 countries each year.

### ***Tainted blood inquiry announced***

<http://news.bbc.co.uk>

Details of a Scottish public inquiry into the infection of NHS patients with hepatitis C and HIV through blood products have been announced.

Health Secretary Nicola Sturgeon said previous government-led inquiries into the issue lacked independence.

Hundreds of people in Scotland, including haemophiliacs, were given the tainted blood in the 70s and 80s.

The previous Holyrood government resisted calls from campaigners for a public inquiry into the issue.

A total of £3m has been earmarked for the independent inquiry, which will be chaired by the former judge and sheriff, Lady Cosgrove and is expected to start hearing evidence towards the end of the year.

It will also specifically look into the deaths of two infected patients, 72-year-old Eileen O'Hara and Rev David Black, 66, in 2003.

Ms Sturgeon told the Scottish Parliament: "The transmission of hepatitis C and HIV through blood and blood products is a tragedy that has blighted the lives of many people in Scotland.

"That is why we are committed to a thorough inquiry to get to the bottom of this.

"We owe an explanation to patients and the public of what took place. We are determined to provide that."

The Scots investigation is expected to look into where NHS blood and blood products previously came from, whether they were effectively screened and whether heat treatment could have been introduced earlier.

It will also probe the practices of the blood transfusion service at the time.

Ms Sturgeon said the events took place at a time when evidence about blood-borne viral infections was more limited - but said, even then, there were indications that tainted blood supplies existed.

"There is no doubt that the people affected and their families deserve nothing less than answers to these questions," she told MSPs

"If they are to achieve any sort of closure, we need to get to the bottom of what has been one of the most tragic episodes in NHS Scotland in the provision of treatment with blood and blood products."

One patient, haemophiliac Robert Mackie, who was diagnosed with hepatitis C and HIV in the early 80s, said an inquiry would provide some answers but would never give him back the life which he said was stolen from him.

He told BBC Scotland: "The day I was told I was infected, my life ended as far as I was concerned. Life as I knew it was over.

"None of us knew of these risks or were even told of these risks."

The Conservatives and Liberal Democrats welcomed the inquiry, as did Labour - although the party questioned what extra benefit it could bring, given a similar investigation was currently under way in England.

**April 24<sup>th</sup>, 2007**

## ***Study shows positive findings in treating patients with advanced hepatitis C***

<http://www.eurekalert.org>

MILAN, ITALY, April 24, 2008 – The hepatitis C therapy peginterferon alfa-2b, when given as low-dose maintenance therapy, can prevent disease progression in certain patients who failed previous interferon-based hepatitis C therapies and have advanced liver disease, according to findings from a large, four-year study presented today at the 43rd annual meeting of the European Association for the Study of the Liver (EASL).

The study, called **COPILLOT (COLchicine versus Peg-Intron LOng-Term)**, showed that low-dose peginterferon alfa-2b was superior to colchicine in improving the disease-free survival of patients with cirrhosis and portal hypertension, especially in patients who stayed on treatment. In the study, more than 40 percent of patients had portal hypertension, a condition of high blood pressure in the major vessel going to the liver from the gastrointestinal tract and which often accompanies liver cirrhosis. However, peginterferon alfa-2b maintenance therapy was not superior to colchicine in patients overall.

“These findings make a strong case for considering low-dose peginterferon alfa-2b as a maintenance therapy in patients with cirrhosis and portal hypertension who have failed hepatitis C eradication therapy,” said principal investigator Nezam Afdhal, M.D., Chief of Hepatology at Beth Israel Deaconess Medical Center (BIDMC) and Associate Professor of Medicine at Harvard Medical School. “While other interferon maintenance therapies have been studied in the past few years in previous interferon nonresponders, these findings show, for the first time, a clinical benefit in a specific population with advanced disease,” he said.

Hepatitis C virus (HCV) infection is transmitted through exposure to infected blood and affects an estimated 4 million individuals in the United States. The current standard treatment, combination therapy with pegylated interferon plus ribavirin for 24 to 48 weeks, can eradicate the virus in about 50 percent of patients. Those who do not respond and have cirrhosis are at far greater risk for developing liver cancer or liver failure, so the development of treatment strategies for these nonresponders is a priority.

Conducted at approximately 40 sites in the United States, the COPILLOT study compared weight-based low-dose peginterferon alfa-2b (subcutaneous injection of 0.5 mcg/kg/wk, one-third the dose used in standard HCV combination therapy) versus colchicine (0.6 mg orally, twice daily), an anti-inflammatory and antifibrotic medication, in 555 chronic hepatitis C patients with

advanced liver fibrosis who previously failed interferon-based therapies. Patient baseline characteristics were well balanced between the two study arms. Over the four years of the randomized study, investigators monitored the patients to determine how many reached a primary endpoint, defined as death, liver transplant, hepatocellular carcinoma (liver cancer), variceal bleeding, or liver failure (increase in Child-Pugh-Turcotte [CPT] by 2 points with ascites, jaundice or encephalopathy). They analyzed their findings for all 555 patients, who received at least one dose of their assigned drug, in two ways: based on all events that occurred during the entire four years of the study, regardless of whether a patient was still taking their assigned drug or not (the “intent-to-treat” or ITT analysis), and based on only the events that occurred while patients were taking their assigned drug (the “on drug” analysis).

The investigators found a primary endpoint was reached by 17.8% (51/286) of patients in the peginterferon alfa-2b group versus 20.4% (55/269) in the colchicine group in the ITT analysis, and by 12.2% (35/286) and 16.0% (43/269) patients, respectively, in the on-drug analysis (treatment differences were not statistically significant). Among patients who had portal hypertension (42.3% and 48.0% of patients in the peginterferon alfa-2b and colchicine groups, respectively), peginterferon alfa-2b therapy resulted in significantly improved event-free survival in both the ITT and on-drug analyses (Wilcoxon  $p = 0.041$  and  $0.028$ , respectively). Further, variceal bleeding, a specific complication of portal hypertension, was almost abolished with peginterferon alfa-2b in both the ITT (10 vs. 1 patients) and the on-drug (10 vs. 0 patients) analyses. In the ITT analysis, hepatocellular carcinoma occurred in 7.7% and 5.9% of patients in the peginterferon alfa-2b and colchicine groups, respectively, a non-significant difference.

Overall, 49% of patients discontinued their medication before the end of the four-year study, with 36% due to failure to comply and 13% due to side effects. Peginterferon alfa-2b was generally well tolerated. Among patients who discontinued due to interferon side effects (17.1%, 49/286), the most common reason (45%, 22/49 patients) was general intolerance to interferon (e.g., due to flu-like symptoms, malaise, and other common interferon side effects).

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*The COPILOT study was supported by Schering-Plough Corporation, manufacturer of peginterferon alfa-2b.*

## **Biolex Therapeutics Researchers Present Locteron(R) Phase 2a Hepatitis C Trial Results at EASL Conference**

<http://www.earthtimes.org>

PITTSBORO, NC -- 04/24/08 -- Biolex Therapeutics, Inc. announced that the results from its SELECT-1 Phase 2a clinical trial of **Locteron®** will be presented today at the 43rd Annual Meeting of the European Association for the Study of the Liver (EASL). As a controlled-release interferon alfa, Locteron is designed to improve patient care through a more favorable side-effect profile compared to existing pegylated interferon products and Albuferon®, each of which lacks a controlled-release mechanism.

SELECT-1 was a twelve-week trial in 32 treatment-naïve patients chronically infected with the genotype-1 variant of the hepatitis C virus. The Phase 2a trial was designed to evaluate four doses of Locteron administered once every two weeks in combination with the antiviral drug

ribavirin. In the SELECT-1 trial, Locteron demonstrated a strong anti-viral response with 100% of the patients in the two highest dose groups achieving early virologic response. Viral kinetic modeling of the SELECT-1 results by Eva Herrmann, Ph.D. of Saarland University, Homburg/Saar, Germany and Stefan Zeuzem, M.D. of JW Goethe-University Hospital, Frankfurt/Main, Germany, demonstrated a statistically significant dose response. Updated results presented at the EASL meeting also included the effect of Locteron on biomarkers and alanine aminotransferase (ALT), each of which showed a dose-dependent response to Locteron.

### **SELECT-1 Results Presented Today at EASL Conference**

The SELECT-1 results will be presented today at the EASL conference in a poster titled "Viral Kinetics during Treatment with a Controlled-Release Recombinant Interferon Alfa-2b in Genotype 1 Chronic Hepatitis C Patients." Anti-viral results for the SELECT-1 trial were as follows:

- The percentage of patients who achieved early virologic response (EVR), defined as at least a two-log reduction in hepatitis C virus, was 100% in the 640 and 480 µg dose cohorts and 88% in the 320 µg dose cohort, compared to 37.5% in the 160 µg dose cohort.
- A clear dose response was observed in the study, and viral kinetic modeling by Drs. Herrmann and Zeuzem demonstrated statistically significant HCV RNA reduction during the entire 12-week treatment period.
- Average viral reduction after 12 weeks of treatment ranged from 4.7 to 4.2 logs for the 640, 480 and 320 µg doses, compared to 1.8 logs for the lowest dose of 160 µg.
- Locteron was generally well tolerated at all doses. There were no serious adverse events in the 160 µg, 320 µg, and 480 µg cohorts. There was one serious adverse event in the 640 µg cohort, a case of otitis, or inflammation of the ear, which resolved.
- Over 90% of the adverse events that were experienced were rated as mild.

The SELECT-1 trial also measured certain biomarkers, the results of which were as follows:

- Locteron resulted in a dose-dependent reduction in alanine aminotransferase (ALT), an enzyme released by the liver into the blood when the liver is damaged.
- Locteron resulted in a dose-dependent increase in oligoadenylate synthetase (OAS) and neopterin, markers commonly associated with the biological effects of interferon alfa.

### **Locteron Overview**

As a controlled-release interferon alfa, Locteron is designed to improve patient care through a more favorable side-effect profile compared to existing pegylated interferon products and Albuferon (albumin-fused interferon), each of which lack a controlled-release mechanism. Locteron combines BLX-883, a recombinant interferon alfa produced by Biolex in its patented LEX System(SM), with PolyActive(TM), an advanced controlled-release drug delivery technology developed by OctoPlus. Locteron is configured to allow dosing once every two weeks, an improvement in patient convenience compared to currently marketed pegylated interferon alfa products that require dosing every week. More importantly, Locteron's controlled-release mechanism results in the gradual release of interferon alfa to patients over the duration of two weeks. This controlled-release mechanism is designed to cover inter-dose troughs which may contribute to the frequency, duration and severity of side effects, including flu-like symptoms, commonly experienced by patients treated with currently marketed pegylated interferons and with Albuferon. Biolex is co-developing Locteron with its partner OctoPlus N.V.

In February 2008, Biolex announced the commencement of patient dosing in a U.S. Phase 2a clinical trial of Locteron in hepatitis C. The U.S. "PLUS" Phase 2a trial is designed to expand upon the favorable results from the SELECT-1 trial reported above and to provide U.S. investigators first-hand experience with Locteron.

Locteron is an investigational therapeutic candidate and has not been approved for sale by the United States Food and Drug Administration or by any international regulatory agency.

## **Pharmasset Adds Two Cohorts to R7128 Hepatitis C Study**

<http://www.earthtimes.org>

*-- Two 4-week cohorts will be enrolled to evaluate R7128 1500mg BID in HCV genotypes 2 and 3 prior non-responders and R7128 1000mg BID in HCV genotype 1 treatment-naive patients --*

PRINCETON, N.J. and MILAN, Italy, April 24 /PRNewswire-FirstCall/ -- Pharmasset, Inc. will enroll two additional cohorts in the on-going Phase 1 study protocol to evaluate 4 weeks of combination therapy with **R7128**. R7128, a prodrug of PSI-6130, is a nucleoside analogue polymerase inhibitor of hepatitis c virus (HCV) that is being developed through Pharmasset's collaboration with Roche.

Cohort 3 will study R7128 1000mg BID in treatment-naive patients with HCV genotype 1. This cohort is intended to provide clinical antiviral activity data in support of pharmacokinetic models from earlier studies. Cohort 4 will study R7128 1500mg BID in patients with HCV genotypes 2 and 3 who did not achieve a sustained virologic response (SVR) with previous interferon-based therapy. Cohorts 3 and 4 will both be dosed in combination with Pegasys (peginterferon alfa-2a) plus Copegus (ribavirin).

Patients in Cohorts 3 and 4 are scheduled to begin dosing by the end of May 2008. Preliminary safety and antiviral activity data from the 4-week combination studies are anticipated during the 3rd quarter of 2008. Cohorts 3 and 4 will be conducted in parallel with the global Phase 2b study preparation activities for R7128. The timing of the Phase 2b study is not dependent upon data from Cohorts 3 and 4.

"Our pharmacokinetic modeling of the 500mg and 1500mg cohorts of R7128 in combination with Pegasys plus Copegus suggests that the 1000mg dose could deliver a rapid virologic response (RVR) rate similar to the 1500mg dose," stated Dr. Michelle Berrey, Pharmasset's Chief Medical Officer. "The confirmatory results from this additional cohort will aid us in selecting the appropriate doses to evaluate in the global Phase 2b study that is being planned to evaluate R7128 in triple combination for up to 12 weeks."

"R7128 is equally potent in vitro against HCV genotypes 1, 2, 3 and 4, and we believe it is clinically and commercially important to test R7128 in patients with these HCV genotypes," stated Schaefer Price, Pharmasset's Chief Executive Officer. "Twenty percent of U.S. HCV-infected patients and approximately 30% of European and Latin American HCV-infected patients have genotypes 2 and 3. These patients are currently treated with 24 weeks of pegylated-interferon plus ribavirin, but 20% of this population fails to achieve an SVR. By potentially addressing this unmet medical need in a patient population for whom the standard of

care is only 24 weeks, we could possibly design shorter clinical trials that may provide a quicker path to the market for R7128."

Separately, the results of the 4-week Phase 1 clinical trial evaluating two oral dose levels of R7128 (500mg and 1500mg) in combination with Pegasys plus Copegus in 50 treatment-naive patients chronically infected with HCV genotype 1 will be presented at the 43rd Annual Meeting of the European Association for the Study of the Liver (EASL) in Milan, Italy on Friday, April 25, 2008 at 11:15 AM ET (US) and 5:15 PM CEST (Milan). The scientific presentation will be available for download in PDF format immediately following the EASL presentation in the "Events & Presentations" section of the Investor Center on Pharmasset's website at <http://investor.pharmasset.com/events.cfm>.

Please see <http://www.clinicaltrials.gov/> or e-mail [clinicaltrials@pharmasset.com](mailto:clinicaltrials@pharmasset.com) for more information.

#### Conference Call

Pharmasset will host a conference call at 1:00 PM ET (US) and 7:00 PM CEST (Milan) on Friday, April 25, 2008 to discuss the addition of two R7128 cohorts, as well as the results of the 4-week combination study of R7128 presented at EASL.

#### Dial-in Information:

US/Canada Toll-Free callers: +1 (877) 545-1490

US/Canada Toll or International Toll callers: +1 (719) 325-4884

Live audio of the conference call will be simultaneously broadcast over the internet via a webcast. To access the live webcast, log on to the "Events & Presentations" section of the Investor Center on Pharmasset's corporate website at <http://investor.pharmasset.com/events.cfm>.

Please connect to the company's website at least ten minutes prior to the start of the presentation to ensure adequate time for a reliable connection and any software download that may be necessary to listen to the webcast. The archived replay of the webcast will be available on the Pharmasset website for two weeks following the conference call.

#### About R7128

R7128 is being developed for the treatment of chronic HCV infection. R7128 is a prodrug of PSI-6130, a cytidine nucleoside analog inhibitor of HCV RNA polymerase. A prodrug is a chemically modified form of a molecule designed to enhance the absorption, distribution and metabolic properties of that molecule. Results from an oral single ascending dose study of PSI-6130 in 24 healthy male volunteers showed that PSI-6130 was generally well tolerated with no serious adverse events in doses up to 3000 mg.

R7128 demonstrated potent, dose-dependent antiviral activity across four prior treatment-failure patient cohorts (n=40) receiving 750 mg or 1500 mg administered either once-daily or twice-daily for 14 days as monotherapy. The greatest mean decrease in HCV RNA from baseline was demonstrated in the patient cohort that received 1500 mg twice-daily, the highest dose of R7128 administered in the study. These patients demonstrated a mean 2.7 log<sub>10</sub> IU/mL (>99%) decrease in HCV RNA. There was no evidence of the development of viral resistance in any dose cohort after 14 days of dosing.

In a 4-week Phase 1 combination study that was conducted in 50 treatment- naive patients chronically infected with HCV genotype 1, R7128 demonstrated potent short-term antiviral activity and was generally safe and well tolerated. Eighty-five percent (85%) of patients receiving R7128 1500mg twice- daily (BID) with Pegasys plus Copegus for 4 weeks achieved undetectable HCV RNA levels with safety and tolerability comparable to placebo with Pegasys plus Copegus.

## ***Why the World Should Ask 'Am I Number 12?'***

<http://www.prnewswire.com>

*- More Than 200 Patient Groups Launch Global Viral Campaign*

<http://www.aminumber12.org> - <http://www.suis-jelenumero12.org> -  
<http://www.souonumero12.org> - <http://www.sonoioilnumero12.org> -  
<http://www.soyelnumero12.org> - <http://www.rakam12.org> -

The World Hepatitis Alliance and over 200 patient groups around the world are asking 'Am I Number 12?' (<http://www.aminumber12.org>) to increase awareness of the shocking statistic that one in 12 people on the planet are living with hepatitis B or hepatitis C and yet the majority of those infected are unaware.

Three weeks ahead of World Hepatitis Day on Monday 19 May, the World Hepatitis Alliance is launching a viral campaign aimed at getting people talking about the fact that approximately 500 million people globally are living with either hepatitis B or C. The World Hepatitis Alliance is asking people to sign-up to <http://www.aminumber12.org> to show support for the campaign but also to receive valuable information about a disease that kills some 1.5 million people a year.

The 'Am I Number 12?' campaign has already kicked off in 64 countries and high-profile campaigns are being coordinated from Sydney to Serbia and from Beijing to Buenos Aires. Charles Gore, President of the World Hepatitis Alliance, said that with 1.5 million people dying every year, chronic viral hepatitis could no longer be ignored. "Through the 'Am I Number 12?' campaign and activities around the world on 19 May we aim to put hepatitis B and C firmly on the global healthcare agenda," Mr Gore said.

Mr Gore continued that unlike other disease areas, awareness of hepatitis B and C remains inexplicably low: "We believe that, unless awareness improves, we won't make any progress in reducing the enormous and largely preventable death toll. Hepatitis B and hepatitis C should have the same profile as HIV/AIDS, malaria and TB and should really be up there alongside those diseases in the WHO's millennium goals."

### **Did You Know?**

- 500 million people worldwide are currently infected with hepatitis B or C
- This is over 10 times the number infected with HIV/AIDS
- Between them, hepatitis B and C kill 1.5 million people a year
- One in every three people on the planet has been exposed to either or both viruses
- Most of the 500 million infected do not know

## **World Hepatitis Day**

World Hepatitis Day will be observed on Monday 19 May and marks a brand new, entirely patient-led initiative. The day has been launched in response to the concern that chronic viral hepatitis has nowhere near the level of awareness nor the political will to tackle it that is seen in HIV/AIDS, TB and malaria. This is despite the fact that the numbers chronically infected with, and annually killed by, hepatitis B and C viruses are on the same scale. 'Am I Number 12?' campaign materials are available in over 40 languages - for logo images, postcards, posters and banner ads please contact the World Hepatitis Alliance at [worldhepday@fleishman.com](mailto:worldhepday@fleishman.com)

## **World Hepatitis Alliance**

World Hepatitis Day is being coordinated by the World Hepatitis Alliance, a newly established Non-Governmental Organisation which represents more than 200 hepatitis B and hepatitis C patient groups from around the world. The World Hepatitis Alliance is governed by a representative board of patient groups from seven world regions: Europe, Eastern Mediterranean, North Africa, North America, South America, Australasia & Western Pacific. For more information visit <http://www.worldhepatitisday.com> on Monday 19 May.

## **Contact Information:**

International - Lorna Croft,  
T: +44-20-7395-7067,  
E: [worldhepday@fleishman.com](mailto:worldhepday@fleishman.com) .

## ***Vertex reports promising hepatitis C drug results***

<http://www.reuters.com>

By Deena Beasley

LOS ANGELES, April 23 (Reuters) - Vertex Pharmaceuticals Inc (VRTX.O: Quote, Profile, Research) on Wednesday said early trial results show that its experimental hepatitis C treatment controlled or eradicated the virus in more than 80 percent of patients for whom previous treatment had failed.

The ongoing study involves only patients with chronic hepatitis C who were unable to achieve control of the serious liver disease with the standard treatment of pegylated interferon and ribavirin.

Vertex said interim results from the open-label trial found that 49 of 60 patients treated with three-times-a-day telaprevir in combination with the other two drugs showed a high rate of viral response after four weeks.

"We are shooting for a cure to the disease," said Kurt Graves, chief commercial officer at Vertex.

The company said the response appears to have been maintained, with no viral breakthrough, in the 36 patients who have completed 4 weeks of treatment and continued out to 8 weeks and in the 16 patients who have continued to 12 weeks of treatment.

"While early, these results are very promising. Patients who have not achieved sustained viral response with prior treatment represent the largest unmet medical need in hepatitis C," Dr. Fred

Poordad, chief of hepatology at Cedars-Sinai's liver disease center in Los Angeles, and the study's lead investigator.

He said only 10 percent to 15 percent of patients have their virus eradicated when re-treated with current therapies.

The trial results were presented in Milan at a meeting of the European Association for the Study of the Liver.

Hepatitis C is a blood-borne disease that can cause chronic liver disease, liver cancer and cirrhosis. It affects roughly 170 million people worldwide.

Side effects of **telaprevir** include fatigue, nausea, headache and rash.

Vertex said nine patients dropped out of the trial before 12 weeks, including five whose viral loads did not drop far enough and two who experienced viral breakthrough. One patient discontinued treatment due to rash and one discontinued due to inflammation of the chest cavity.

Telaprevir is designed to block HCV protease, an enzyme essential for the virus to replicate.

Earlier trials in previously-untreated patients found that the drug eradicated the virus in more than 60 percent of patients -- a rate about 20 percent higher than that seen with current therapies.

Graves said Vertex is also testing a twice-daily regimen of telaprevir and expects to have interim results in May from a 440-patient trial testing the drug in patients not cured by prior interferon-based therapy.

The company also expects to complete late this year enrollment in a pivotal phase 3 trial of telaprevir in treatment-naive patients. (Editing by Carol Bishopric)

### ***Officials Say 10,000 More at Risk in Hepatitis Outbreak***

<http://www.kolotv.com>

LAS VEGAS (AP) - The Southern Nevada Health District says another 10,000 people may have been exposed to hepatitis C at an outpatient medical clinic in Las Vegas.

District officials announced the updated estimate at a meeting Thursday. It brings to 50,000 the number of people who authorities say might have been infected with hepatitis or HIV through the Endoscopy Center of Nevada.

Officials say a review of health insurance records led to the higher number.

The health district began notifying more than 40,000 patients in February that they might have been exposed to the potentially fatal viruses.

Authorities blame the infections on the reuse of needles and vials of medication on multiple patients, and say they've traced eight acute cases of hepatitis C to two clinics.

April 25<sup>th</sup>, 2007

## **Gilead's hepatitis B drug gets EU marketing approval**

<http://www.bizjournals.com>

*San Francisco Business Times*

Gilead Sciences Inc. said Friday the European Commission gave its OK to sell Viread, a treatment for chronic hepatitis B.

Foster City-based Gilead (NASDAQ:GILD) said the authorization covers all 27 member states of the European Union.

Viread is taken once a day and blocks the hepatitis B virus DNA polymerase, the enzyme that is necessary for the virus to replicate in liver cells.

The product was recently approved for the treatment of chronic hepatitis B in Turkey and New Zealand. Marketing applications being reviewed by the United States, Canada and Australia.

## **Pharmasset Presents Results of 4-Week Combination Study of R7128 for the Treatment of Chronic Hepatitis C**

<http://biz.yahoo.com>

- *85% of patients achieve undetectable HCV RNA levels following 4 weeks of treatment with R7128 1500mg BID with Pegasys(R) plus Copegus(R) -*
- *Safety and tolerability comparable to placebo administered with Pegasys plus Copegus -*
- *EASL presentation available on Pharmasset website -*
- *Conference call scheduled for Friday, April 25, 2008 at 1:00 PM ET (US) and 7:00 PM CEST (Milan) -*

PRINCETON, N.J. and MILAN, Italy, April 25 /PRNewswire-FirstCall/ -- Pharmasset, Inc. (Nasdaq: VRUS - News) announces the results of a 4-week Phase 1 clinical trial evaluating two oral dose levels of R7128 in combination with Pegasys (pegylated interferon) plus Copegus (ribavirin) in 50 treatment-naive patients chronically infected with hepatitis C virus (HCV) genotype 1. R7128, a prodrug of PSI-6130, is a nucleoside analogue polymerase inhibitor of HCV that is being developed through Pharmasset's collaboration with Roche. The results of this study were presented today at the 43rd Annual Meeting of the European Association for the Study of the Liver (EASL) being held from April 23-27, 2008 in Milan, Italy.

In this study, R7128 demonstrated potent short-term antiviral activity and was generally safe and well tolerated. Eighty-five percent (85%) of patients receiving R7128 1500mg twice-daily (BID) with Pegasys plus Copegus for 4 weeks achieved undetectable HCV RNA levels with safety and tolerability comparable to placebo with Pegasys plus Copegus.

Dr. John McHutchison, professor of medicine at Duke University Medical Center and a clinical investigator for this study, stated, "R7128, in combination with Pegasys plus Copegus, has demonstrated Rapid Virologic Response (RVR) percentages in a 4-week study that are similar to HCV protease inhibitors and has an encouraging short-term clinical safety profile. Longer-term studies of R7128 with Pegasys plus Copegus are needed to provide additional information about its potential to improve sustained virologic response (SVR) rates for HCV patients."

### **R7128 4-week Combination Study Overview**

The 4-week Phase 1 combination clinical trial was a multiple center, observer-blinded, randomized and placebo-controlled study that was conducted in 50 treatment-naive patients chronically infected with HCV genotype 1. The primary objective was to assess the safety, tolerability and pharmacokinetics of R7128 in combination with Pegasys plus Copegus. The secondary objective was to evaluate the change in HCV RNA after 4 weeks of treatment.

The study investigated two oral dose levels of R7128, 500mg and 1500mg, each administered twice-daily (BID) with once-weekly injections of Pegasys plus Copegus BID. Each cohort of 25 patients was comprised of 20 patients receiving R7128 and 5 patients receiving placebo with Pegasys plus Copegus.

### **Antiviral Activity Summary**

	<b>Placebo + Pegasys plus Copegus (n=10)</b>	<b>R7128 500mg + Pegasys plus Copegus (n=20)</b>	<b>R7128 1500mg + Pegasys plus Copegus (n=20)</b>
Mean Decrease in HCV RNA (log <sub>10</sub> IU/mL) at 4 Weeks	-2.95	-3.82	-5.12
Percentage of Patients with Undetectable HCV RNA (<15 IU/mL) at 4 Weeks (RVR)	10%	30%	85%

Potent antiviral activity was demonstrated following 4 weeks of treatment with R7128 1500mg BID with Pegasys plus Copegus. These patients achieved a mean 5.12 log<sub>10</sub> IU/mL decrease in HCV RNA and 85% (17 of 20) had undetectable levels of HCV RNA (<15 IU/mL), or RVR. Following 4 weeks of treatment with R7128 500mg BID with Pegasys plus Copegus, patients achieved a mean 3.82 log<sub>10</sub> IU/mL decrease in HCV RNA and 30% (6 of 20) had RVR. Following 4 weeks of treatment with placebo with Pegasys plus Copegus, patients achieved a mean 2.95 log<sub>10</sub> IU/mL decrease in HCV RNA and 10% (1 of 10) had RVR. The baseline HCV RNA levels for all patients in the study were greater than 6.3 log<sub>10</sub> IU/mL and were similar across all study groups.

### **Safety Summary**

Safety and tolerability for the 4-week treatment period were similar for R7128 with Pegasys plus Copegus compared to placebo with Pegasys plus Copegus. There were no serious adverse events reported during the 4-week treatment period, and most of the adverse events reported were of mild to moderate intensity. The most common adverse events, reported in 15% or greater of patients in any treatment group during the 4-week treatment period, were headache, injection site

reaction, myalgia, fatigue, chills, rash, nausea, diarrhea, arthralgia, pyrexia, dizziness, dyspepsia and pruritis. The frequency and severity of these adverse events, as well as any general body system observations, were generally similar to clinical experience with the standard of care for HCV, pegylated interferon plus ribavirin.

Grade 3/4 neutropenia was observed in 30% of the placebo patients and in 10% to 15% of the R7128 patients in each active dosing cohort. Grade 3 changes in hemoglobin were observed in 10% of the placebo patients and in 15% of the R7128 patients. There were no clinically significant changes in other hepatic, renal, or other safety laboratory parameters, vital signs, or electrocardiograms.

Overall, there was no clinical evidence of any major organ toxicities related to R7128. One patient in the active treatment group discontinued the study during the 4 week treatment period due to lower-gastrointestinal adverse events. At the time of study discontinuation, this patient had undetectable HCV RNA. R7128 was generally safe and well-tolerated when administered for 4 weeks in combination with Pegasus plus Copegus in patients with HCV genotype 1.

Please see [www.clinicaltrials.gov](http://www.clinicaltrials.gov) or e-mail [clinicaltrials@pharmasset.com](mailto:clinicaltrials@pharmasset.com) for more information.

### **Conference Call**

Pharmasset will host a conference call at 1:00 PM ET (US) and 7:00 PM CEST (Milan) on Friday, April 25, 2008 to discuss the R7128 500mg and 1500mg combination study results, as well as the addition of two R7128 cohorts to the on-going Phase 1 protocol.

#### *Dial-in Information:*

US/Canada Toll-Free callers: +1 (877) 545-1490

US/Canada Toll or International Toll callers: +1 (719) 325-4884

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### **About R7128**

R7128 is being developed for the treatment of chronic HCV infection. R7128 is a prodrug of PSI-6130, a cytidine nucleoside analog inhibitor of HCV RNA polymerase. A prodrug is a chemically modified form of a molecule designed to enhance the absorption, distribution and metabolic properties of that molecule. Results from an oral single ascending dose study of PSI-6130 in 24 healthy male volunteers showed that PSI-6130 was generally well tolerated with no serious adverse events in doses up to 3000 mg.

R7128 demonstrated potent, dose-dependent antiviral activity across four prior treatment-failure

patient cohorts (n=40) receiving 750 mg or 1500 mg administered either once-daily or twice-daily for 14 days as monotherapy. The greatest mean decrease in HCV RNA from baseline was demonstrated in the patient cohort that received 1500 mg twice-daily, the highest dose of R7128 administered in the study. These patients demonstrated a mean 2.7 log<sub>10</sub> IU/mL (>99%) decrease in HCV RNA. There was no evidence of the development of viral resistance in any dose cohort after 14 days of dosing.

## ***Data On Investigational Compounds Being Co-Developed By Tibotec For The Treatment Of Chronic Hepatitis C Presented At EASL 2008***

<http://www.medicalnewstoday.com>

Tibotec BVBA, a global pharmaceutical company dedicated to the discovery and development of innovative drugs that fight infectious diseases, is now building a portfolio of novel antiviral therapies to treat hepatitis C virus (HCV). The investigational protease inhibitors (PI), telaprevir (VX-950) and TMC435350, are being co-developed by Tibotec with Vertex and Medivir, respectively. Data on these compounds will be presented at the 43rd Annual Meeting of the European Association for the Study of the Liver (EASL) in Milan, Italy.

According to the World Health Organization, an estimated 170 million persons globally are chronically infected with HCV and three to four million persons are newly infected each year.[i] Chronic infection with HCV, a viral infection of the liver, can lead to cirrhosis and liver cancer, and is the most common cause of liver transplant in Europe.[ii],[iii] The current standard of care for HCV patients, treatment with pegylated interferon combined with ribavirin, is effective in thirty to fifty percent of patients with genotype-1 HCV, the most common type globally.[iv] However, treatment with this regimen can cause significant side effects and no effective treatment regimen has been identified for those patients that have failed treatment, sometimes known as non-responders.[v],[vi] The development of new therapies, particularly direct antivirals with different modes of action, will allow HCV patients to undergo a more effective treatment regimen.[vii],[viii]

"Our goal is to develop and bring to market new direct antivirals for the treatment of hepatitis C that have significant advantages over the existing standard of care," said Roger Pomerantz, MD, President of Tibotec Research and Development.

As a global virology leader committed to patient care, Tibotec uses innovative science and expertise and works with partners to research, develop, manufacture, and market drugs of unmet need. To date, Tibotec has brought to market PREZISTATM (darunavir), an antiretroviral medication for treatment-experienced patients with HIV, and has submitted a marketing application for its second HIV medication, INTELENCETM (etravirine), to the European Agency for the Evaluation of Medicinal Products (EMA). Its promising pipeline comprises potential treatments for infectious diseases including HIV, tuberculosis, and HCV.

### **Telaprevir: Key Presentations at EASL**

Data from four abstracts on telaprevir, which is in phase III development, will be presented in poster and oral presentations at EASL. Highlights include early results from VX06-950-107, an ongoing, open-label study to evaluate the antiviral response to treatment with telaprevir, combined with pegylated interferon alfa-2a (Peg-IFN) and ribavirin (RBV), in patients who have

failed treatment with Peg-IFN/RBV in any of the three PROVE trials will be presented as a late-breaker poster. An interim analysis examined a small subset of patients that included non-responders and relapsers. These are the first data to be presented on the use of telaprevir in patients who have previously failed previous Peg-IFN/RBV therapy.

Further results from PROVE-1 (U.S.) and PROVE-2 (Europe), two randomised, placebo-controlled Phase II studies of telaprevir combined with Peg-IFN and with or without RBV in treatment-naïve patients with HCV genotype 1, will be presented in oral sessions on Thursday, 24 April and Friday, 25 April, respectively.

Telaprevir is currently being studied in Phase III clinical trials in treatment-naïve patients; a Phase III clinical trial in patients that have previously failed treatment will begin later this year. Tibotec has the right to develop and commercialise telaprevir in Europe, South America, the Middle East, Africa, India, Australia and New Zealand; Vertex will commercialise telaprevir in the U.S., Canada and Mexico.

### **TMC435350: First Results in Patients**

In addition, data from a placebo controlled, double-blind Phase I study of TMC435350 will be presented in an oral session on Friday, 25 April. This study examined the safety, tolerability and pharmacokinetics of TMC435350 in healthy volunteers and also examined antiviral activity of the drug in a small number of HCV patients who had previously failed treatment. These are the first data to be presented on the use of TMC435350 in hepatitis C patients.

Tibotec and Medivir discovered TMC435350 through a drug discovery collaboration. Tibotec has the right to commercialise the compound throughout the world, excluding the Nordic countries. A Phase IIa proof-of-concept trial is ongoing in Europe and is currently recruiting patients.

### **About Tibotec**

Tibotec BVBA, is a pharmaceutical research and development company. The Company's main research and development facilities are in Mechelen, Belgium with offices in Yardley, PA and Cork, Ireland. Tibotec is dedicated to the discovery and development of innovative HIV/AIDS and hepatitis C drugs, and anti-infectives for diseases of high unmet medical need.

<http://www.tibotec.com>