

HCV ADVOCATE WEEKLY NEWS REVIEW

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

*Alan Franciscus
Editor-in-Chief*

Week Ending: February 16th 2008

In This Issue:

- [Schering-Plough, OraSure Tech collaborate on oral hepatitis C test outside U.S.](#)
- [SciClone, Sigma-Tau Announce Promising Interim Results From Phase 3 Hepatitis C Trial - Quick Facts](#)
- [Investigators at Georgetown University release new data on cancer](#)
- [FibroScan® for Hepatitis](#)
- [Democrats Threaten to Hold HHS Head in Contempt Over Ketek Probe](#)
- [Enhanced Liver Fibrosis Panel Aids Testing for Nonalcoholic Fatty Liver Disease](#)
- [Vertex Shares Fall on Costs](#)
- [Presidio Pharmaceuticals And Numerate Announce Research Collaboration To Identify Improved Hepatitis C Therapeutics](#)
- [Too Much Fast Food and Too Little Exercise Harm the Liver](#)
- [Husband blast on Anita's bug](#)
- [Committee votes to mandate organ donor decision](#)
- [GenOdyssey Receives Notice of Allowance from U.S. Patent Office for Improved Interferon-Alpha Aimed at Hepatitis C](#)
- [Sorafenib Plus Doxorubicin May Offer Better Time to Progression Than Doxorubicin Alone in Advanced Hepatocellular Carcinoma: Presented at ICACT](#)
- [Report increases hepatitis C exposure cases to 8,896](#)
- [CROI: Choice of nucleoside analogue in co-infection: tenofovir associated with better response to HCV therapy](#)

February 11th, 2007

Schering-Plough, OraSure Tech collaborate on oral hepatitis C test outside U.S.

<http://www.forbes.com>

NEW YORK (Thomson Financial) - Schering-Plough Corp. and OraSure Technologies Inc. Monday agreed to collaborate on the development and promotion of an oral hepatitis C virus (HCV) test outside the U.S.

The test will use OraSure's OraQuick technology platform. The hepatitis C test is limited to professional use and is not available over the counter.

The technology used is similar to OraQuick, an OraSure product that detects HIV within 20 minutes. It can be applied orally or on blood samples.

Under the agreement Schering-Plough (nyse: SGP - news - people) will reimburse OraSure for certain development costs and will provide payments to OraSure based on the achievement of certain regulatory and commercial milestones in international markets. Schering-Plough will provide promotional support while OraSure will make all sales and retain the rights to market and sell the test in all markets throughout the world.

The agreement builds upon the existing collaboration announced in January 2007 to develop and promote a rapid oral HCV test in the U.S. physicians' office market.

'We believe the global market opportunity for a rapid HCV test is significant and this expansion of our collaboration with Schering-Plough should help drive the adoption of this important product around the world,' OraSure said.

OraSure is a Bethlehem, Pa.-based company that specializes in oral fluid specimen collection devices and diagnostic products. Its stock closed Friday at \$7.61.

Shares of Schering-Plough, a Kenilworth, N.J.-based advanced drug therapy company, closed Friday at \$19.77.

SciClone, Sigma-Tau Announce Promising Interim Results From Phase 3 Hepatitis C Trial - Quick Facts

<http://www.tradingmarkets.com>

(RTTNews) - SciClone Pharma., Inc. (SCLN | news | PowerRating | PR Charts) and Sigma-Tau announced promising blinded interim data from a large, randomized phase 3 clinical trial evaluating **ZADAXIN** in combination with pegylated interferon alpha and ribavirin as a treatment for patients with hepatitis C virus, or HCV, who have not responded to prior therapy with pegylated interferon alpha and ribavirin. [According to *Reuters*, 171 out of 553 total patients responding to treatment at the end of 48 weeks of therapy.] The company said that the



full unblinded data from the trial would be available in the third quarter of 2008.

The primary endpoint of the trial is sustained virological response, defined as the absence of HCV RNA measured at week 72, which is the end of the 24-week observation period. The secondary endpoints are normalization of ALT, an enzyme that when present in increased levels is an indicator of inflammation or damage of the liver, measured at the end of weeks 48 and 72, absence of HCV RNA measured at week 48, and an improvement in liver biopsy.

Investigators at Georgetown University release new data on cancer

<http://www.newsrx.com>

Hepatitis Weekly

According to recent research from the United States, "Hepatocellular carcinoma (HCC) represents an important public health problem in Egypt where up to 90% of HCC cases are attributable to hepatitis C viral (HCV) infection. Serum alpha-fetoprotein is elevated in only similar to 60% of HCC patients."

"The development of effective markers for the detection of HCC could have an impact on cancer mortality and significant public health implications worldwide. The objective of our study was to assess six candidate markers for detection of HCC identified by mass spectrometric analysis of enriched serum. The study examined 78 HCC cases and 72 age- and gender-matched cancer-free controls recruited from the Egyptian population. Matrix-assisted laser desorption-ionization time-of-flight mass spectrometric analysis of enriched low-molecular weight fraction of serum was used for identification of the candidate markers. Our analyses show that all six candidate markers are associated with HCC after adjustment for important covariates including HCV and hepatitis B viral infections. The marker candidates are independently predictive of HCC with areas under the receiver operating characteristic (AuROC) curve ranging from 63-93%. A combination of the six markers improves prediction accuracy to 100% sensitivity, 91% specificity and 98% AuROC curve in an independent test set of 50 patients. Two of the candidate markers were identified by sequencing as fragments of complement C3 and C4," wrote R. Goldman and colleagues, Georgetown University.

The researchers concluded: "A set of six peptides distinguished with high prediction accuracy HCC from controls in an Egyptian population with a high rate of chronic HCV infection. Further evaluation of these marker candidates for the diagnosis of HCC is needed.'."

Goldman and colleagues published their study in *Carcinogenesis* (Candidate markers for the detection of hepatocellular carcinoma in low-molecular weight fraction of serum. *Carcinogenesis*, 2007;28(10):2149-2153).

For additional information, contact R. Goldman, Georgetown University, Lombardi Comprehensive Cancer Center, 3970 Reservoir Rd. NW, Washington, DC 20057, USA.

FibroScan® for Hepatitis

<http://www.hoinews.com>

By Jen Christensen

Viral Hepatitis

Viral hepatitis is an inflammation of the liver caused by infection with a virus. Two important types are hepatitis B and hepatitis C.

Hepatitis B

Hepatitis B (HBV) is typically transmitted through contact with contaminated body fluids, such as during sexual intercourse, sharing of contaminated drug needles or from exposure to open wounds, blood or secretions from an infected person. If a pregnant woman has hepatitis B, the baby can acquire the infection during birth.

Most infections with HBV are acute (last for a limited period of time). However, about 5 percent of infected adults develop chronic (long-lasting) infections. The American Liver Foundation estimates about 1.4 million Americans are currently infected with chronic HBV. Over time, chronic infection can lead to liver scarring (fibrosis) and cirrhosis (serious irreversible scarring). Some patients will eventually develop liver failure or liver cancer.

Hepatitis C

Hepatitis C (HCV) is transmitted through contact with contaminated blood. In the past, people could acquire the infection after receiving a transfusion of blood or blood product containing the virus. Now there's a test to screen blood for HCV. Currently, the most common methods of HCV transmission are through sharing of contaminated needles used for illicit drugs, acupuncture, tattooing or piercing. Healthcare workers may become infected if they are accidentally stuck with a contaminated needle or come into contact with contaminated blood.

The American Liver Foundation estimates about 4 million Americans have HCV. About 75 to 80 percent of those who are infected develop chronic infection. 20 percent of chronic infections lead to liver cirrhosis. Researchers say HCV is the leading reason for a liver transplant in the U.S. Each year, more than 10,000 Americans die from complications related to HCV infection.

Monitoring the Progression of Viral Hepatitis

Only a small number of patients with chronic hepatitis will develop liver cirrhosis, liver failure or liver cancer. But there is no way to predict which patients will progress. Many patients with liver damage don't have any signs until the disease has caused serious, irreversible damage. So doctors rely on liver biopsies to measure the amount of fibrosis, or scarring. Patients with more fibrosis may need more aggressive treatment to stem the damage to the liver.

In a liver biopsy, the doctor makes a small incision on the right side of the body, near the rib cage. A biopsy needle is inserted through the cut and into the liver. Then a small sample of the liver is removed. The tissue is sent to a lab for analysis. The lab technician can estimate the degree of liver damage by looking at the amount of scar tissue in the biopsy sample.

FibroScan® for the Liver

Researchers are testing a device, called FibroScan®, which uses ultrasound elastography to



assess liver health. An ultrasound transducer with a vibrating unit is placed over the patient's abdomen. The vibrating transducer emits an elastic sound wave, then calculates the speed at which it passes through the liver. The velocity of the wave as it spreads is a measure of liver stiffness, or fibrosis. The faster the wave spreads, the stiffer, or harder the liver, which in turns means a greater amount of liver fibrosis.

Researchers are now confirming the efficacy of FibroScan's ability to measure the degree of liver fibrosis in patients with HBV and HCV. Patients who are scheduled for a liver biopsy will have the FibroScan followed by their regular biopsy. The results will be compared to track the diagnostic accuracy of FibroScan.

Bruce Bacon, M.D., a Gastroenterologist with St. Louis University School of Medicine, says although biopsies are typically only done every four to five years, they are an invasive procedure and can be painful. The FibroScan doesn't require any incisions or needles and can be repeated as necessary to follow a patient's progression. The study is also taking place in Boston, MA and Durham, NC. For more information log onto <http://www.clinicaltrials.gov> . Then type the trial identification number in the search box: NCT00125762.

AUDIENCE INQUIRY

For information about the clinical trial, log onto <http://www.clinicaltrials.gov> . Then type the trial identification number in the search box: NCT00125762.

For information about the FibroScan® technology:

<http://www.echosens.com>

For general information on hepatitis B or C:

- American Liver Foundation, <http://www.liverfoundation.org>
- Centers for Disease Control and Prevention, <http://www.cdc.gov>
- HCV Advocate, <http://www.hcvadvocate.org>
- Hepatitis Foundation International, <http://www.hepfi.org>
- National Institute of Diabetes and Digestive and Kidney Diseases, <http://www.niddk.nih.gov>

February 13th, 2007

Democrats Threaten to Hold HHS Head in Contempt Over Ketek Probe

<http://www.therapeuticsdaily.com>

WASHINGTON_ Democrats in the U.S. House of Representatives are threatening to hold a member of President George W. Bush's Cabinet in contempt for not turning over documents in a probe of a Sanofi-Aventis antibiotic.

The threat issued Tuesday by Bart Stupak and John Dingell is the latest turn in a year-old investigation of the Sanofi drug, which was linked to death and liver failure in 2006. The Michigan Democrats allege that the Food and Drug Administration approved Ketek despite knowing a major safety study of the drug was plagued by faulty data.

Dingell, who chairs the House Energy and Commerce Committee, said he would support holding Health and Human Services Secretary Michael Leavitt in contempt for refusing to turn over FDA briefing documents subpoenaed by the committee. Leavitt oversees health care agencies including the FDA, which is responsible for the safety of medicines sold in the United States.

The documents were used to prepare FDA Commissioner Andrew von Eschenbach for his appearance before lawmakers last year. Von Eschenbach testified the FDA did not use the flawed safety study to approve Ketek. Dingell and other Democrats say that statement may be untrue.

"What is in those briefing books that he does not want either my Republican colleagues or our side to see? Is there evidence of perjury?" asked Dingell.

Lawmakers heard from three government staffers Tuesday who had to be subpoenaed because the Bush administration refused to let them testify.

Robert West, an FDA agent who first investigated Ketek, said he tried to get permission in 2002 to look into whether Aventis was aware of fraudulent data when it submitted the study. West said his request was blocked by senior FDA officials, although he said he did not know which ones.

FDA eventually issued a warning letter to Sanofi in 2007 over its handling of the trial. The agency found that several physicians hired by Aventis falsified data in the safety study.

"A catastrophic failure" was how another FDA investigator, Douglas Loveland, described the company's handling of the study.

"The decision-making process Aventis used to investigate these problems was illogical and ineffective and it could have led them to come to the wrong conclusion," Loveland told House lawmakers.

The investigator stopped short of saying Aventis, Sanofi-Aventis' corporate predecessor, knew the results were false when they submitted them but said it "should have known." Loveland said the results contained all the hallmarks of sham data, including forged signatures and crossed out information.

Sanofi President for Research and Development Paul Chew testified that the company submitted the study in "good faith."

The company was not able to spot the fake patient results, Chew said, but has since put in place extra steps to verify data.

Ketek, approved in 2004, received FDA's most serious warning last February after reports of liver failure appeared. The drug was approved originally to treat sinus infections, but FDA said it should be used only for pneumonia.

On the Net:

Sanofi-Aventis: <http://www.sanofi-aventis.com/>

FDA: <http://www.fda.gov/>

Enhanced Liver Fibrosis Panel Aids Testing for Nonalcoholic Fatty Liver Disease

www.medscape.com

Laurie Barclay, MD

February 5, 2008 — The Enhanced Liver Fibrosis (ELF) panel, a new method for testing for nonalcoholic fatty liver disease (NAFLD), may help reduce the need for liver biopsies by up to 88%, according to the results of a study reported in the February issue of *Hepatology*.

"The detection of fibrosis within [NAFLD] is important for ascertaining prognosis and the stratification of patients for emerging therapeutic intervention," write Indra Neil Guha, from the University of Southampton, United Kingdom, and colleagues. "We validated the Original European Liver Fibrosis panel (OELF) and a simplified algorithm not containing age, the [ELF], in an independent cohort of patients with NAFLD. Furthermore, we explored whether the addition of simple markers to the existing panel test could improve diagnostic performance."

In a validation study including 196 consecutively recruited patients from 2 centers, the investigators used receiver operator curves, predictive values, and a clinical utility model to compare the diagnostic accuracy of the discriminant scores of the ELF panel, simple markers, and a combined panel. Simple markers included age, body mass index, presence of diabetes or impaired fasting glucose, aspartate aminotransferase/alanine aminotransferase ratio, platelet count, and serum albumin level.

Area under the curve (AUC) for the ELF panel was 0.90 for distinguishing severe fibrosis, 0.82 for moderate fibrosis, and 0.76 for no fibrosis. When the algorithm was simplified by removing age, there was no change in diagnostic performance.

Adding simple markers to the panel improved diagnostic performance, with AUCs of 0.98 for the detection of severe fibrosis, 0.93 for moderate fibrosis, and 0.84 for no fibrosis. Using ELF for the diagnosis of severe fibrosis, 82% of liver biopsies could potentially be avoided, according to the clinical utility model, vs 88% using the combined panel.

"The ELF panel has good diagnostic accuracy in an independent validation cohort of patients with NAFLD," the study authors write. "The addition of established simple markers augments the diagnostic performance across different stages of fibrosis, which will potentially allow superior stratification of patients with NAFLD for emerging therapeutic strategies."

Study limitations include sample selected from a tertiary care setting and representing a more severe disease spectrum, and lack of generalizability to other healthcare settings.

"The true potential of serum markers may not be realized until longitudinal studies measuring serum markers against clinical outcomes are published," the study authors conclude. "The ability to measure disease progression, regression, and response to treatment by serial measurement of serum markers would give clinicians valuable information to aid management decisions."

Some of the authors report various conflicts of interest with iQur Ltd. and/or Bayer/Siemens.

Vertex Shares Fall on Costs

<http://www.chron.com>

NEW YORK — Shares of Vertex Pharmaceuticals Inc. sunk to their lowest level in several years as costs widened the company's fourth-quarter loss and played a factor in a 2008 outlook below Wall Street expectations.

The stock fell \$1.07, or 5.9 percent, to close at \$17.41, but hit \$16.04 earlier in the session. That marked a low point last reached in August of 2005.

The company is moving its lead drug candidate, telaprevir for hepatitis C, into late-stage development in March and said it is ramping up spending for the program. Telaprevir development costs were a key factor in the widened fourth-quarter loss. Vertex is also offering 6 million shares of common stock in a public offering along with \$250 million in senior notes.

Wall Street took a mixed view on the company Tuesday, with several analysts cautious over increased spending while maintaining a positive outlook for telaprevir.

"While we expect growing competition, we believe that Vertex has established a leadership position in what could be a multibillion dollar class (of drugs)," Goldman Sachs analyst Meg Malloy said in a note to investors. "While there is more to the pipeline, we expect hepatitis C (study) progress to be the primary valuation driver."

She reaffirmed a "Buy" rating and lowered her price target to \$41 from \$43, citing the company's plan for a stock sale, which would increase share count.

BMO Capital Markets analyst Jason Zhang reaffirmed a "Outperform" rating with a \$40 price target, citing confidence that an ongoing Phase IIb clinical trial, called Prove-3, could serve as a rapid way to ask for Food and Drug Administration approval. The stock's main driver, he said, will be the company's ability to produce positive data in the upcoming Prove-3 study.

Though the study has a good chance of success, he added, costs will continue to be a factor for the company, and it might have to seek additional funding from Wall Street.

Meanwhile, Deutsche Bank-North America analyst Jennifer Chao reaffirmed a "Buy" rating and \$44 price target but cast doubt over whether the ongoing study could be used to apply for telaprevir approval. Both the ongoing and planned studies could show meaningful, but divergent results, she said.

Presidio Pharmaceuticals And Numerate Announce Research Collaboration To Identify Improved Hepatitis C Therapeutics

<http://www.medicalnewstoday.com>

Presidio Pharmaceuticals, Inc., a specialty pharmaceutical company focused on developing and commercializing novel, small molecule compounds for the treatment of HIV-1 and HCV and Numerate, Inc., a biotechnology company with a proprietary drug engineering platform, announced today that they have entered into a research collaboration to discover and develop novel small molecule inhibitors of hepatitis C virus (HCV). Terms of the collaboration and the specific HCV target were not disclosed.

"I am very pleased to have entered into this agreement," stated Dr. Richard Colonno, Chief Scientific Officer of Presidio Pharmaceuticals. "Numerate has a very promising computational approach that we believe will help expand our HCV portfolio in a highly competitive area encumbered by many patents. Numerate's drug engineering process addresses the key design criteria in parallel with a focus on delivering advanced lead compounds quickly. The process accelerates the discovery and design of novel leads and reduces the time and cost needed to advance compounds into clinical trials."

"We look forward to working with Presidio to deliver proprietary, potent, and selective small molecule leads, enabling them to rapidly identify clinical development candidates," stated Guido Lanza, Chief Executive Officer of Numerate. "We anticipate a true synergistic working relationship with Presidio, working directly with their scientific team to provide lead and backup molecules for the HCV collaboration."

About Presidio Pharmaceuticals

Presidio Pharmaceuticals, Inc. is a specialty pharmaceutical company focused on discovering, licensing, developing and commercializing novel therapeutics for viral infections, including HIV-1 and HCV. Presidio has raised over \$27 million in financing from Panorama Capital (formerly JP Morgan Partners), Baker Brothers Investments, Bay City Capital, Ventures West, Nexus Medical Partners, and Sagamore Bioventures. For more information, please visit our website at <http://www.presidiopharma.com>.

About Numerate

Numerate is a privately held biotechnology company that has developed and extensively validated a drug engineering platform that rapidly and cost-effectively delivers small molecule therapeutics optimized for efficacy, safety, and patentability. Numerate applies this technology to design and develop small molecule drugs in collaboration with a variety of partners and in the advancement of proprietary therapeutic programs including a multi-targeted therapy for type II diabetes and cardiovascular disease.

<http://www.numerate.com>

February 14th, 2007

Too Much Fast Food and Too Little Exercise Harm the Liver

<http://www.newswise.com>

Newswise — Too much fast food and too little exercise can harm the liver, reveals a small study published ahead of print in the journal *Gut*.

The findings are based on 18 slim, healthy people (12 men and six women) who took a “fast food challenge” for four weeks, and a comparison group, matched for age and sex, who ate a normal diet.

The fast food group restricted their levels of physical activity to not more than 5000 daily steps and ate at least two fast food meals, preferably in well known outlets, every day.

The aim was to double calorific intake and increase total body weight by between 10% and 15% to see if these had any impact on their liver health.

Blood samples were taken before the challenge began and then at regular intervals throughout the study period, to check on their liver enzyme and fat levels.

Liver damage is often identified by symptomless increases in enzymes, of which alanine aminotransferase (ALT) is one.

Usually, higher than normal ALT levels are found in people who regularly drink large amounts of alcohol or who have been infected with the hepatitis C virus. But in a significant proportion of people, there is no obvious explanation.

Too much fat in the liver also indicates damage, and is known as “fatty liver.”

At the end of the four weeks, those in the fast food group had put on an average of 6.5 kg. Five increased their weight by 15%, and one person put on an extra 12 kg in just two weeks.

Sharp increases in ALT occurred after just one week on the fast food diet, and more than quadrupled from an average of 22 U/l to of 97 U/l over the entire period.

In 11 people ALT rose to levels indicative of liver damage. The increases were linked to weight gain and especially higher sugar and carbohydrate intake.

Only one participant developed “fatty liver,” but test results from the other participants showed a steep rise in fat content in their liver cells, which is associated with insulin resistance.

Insulin resistance is associated with the metabolic syndrome, a collection of biochemical abnormalities which are linked to an increased risk of diabetes and cardiovascular disease.

No such changes were seen among those who continued to eat their normal diet.

Click here to view the paper in full: <http://press.psprings.co.uk/gut/february/gt131797.pdf>

Husband blast on Anita's bug

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

DAME Anita Roddick’s widower has marked the anniversary of her bombshell announcement that she had hepatitis C – by slamming Government inaction over the killer virus.

Gordon, 65, said: "Letting people die because you can't be bothered to put proper services in place is totally unacceptable."

It is thought 500,000 Brits carry hepatitis C but don't realise.

And the longer it goes undetected, the greater the risk of fatal liver damage or cancer.

In 2004 the Government launched an action plan to tackle the bug.

But an audit out today shows six out of ten primary care trusts are still failing to implement it.

Body Shop founder Dame Anita died last September, aged 64, seven months after revealing she had caught hepatitis C from a blood transfusion in 1971.

And this will be the first Valentine's Day in 40 years when her husband Gordon will be without her.

Blasting the Government on hepatitis C, he added: "It's a scandal. Anita wanted us to be the best in the world at tackling this but we're far behind France, Germany and Italy."

And he has no doubt what her response to the damning audit would be. "B*****s!"

He added: "Anita would say, 'Wake up! Hep C is slowly killing hundreds of thousands in the UK.'"

Call the Hepatitis C Trust helpline on 0870 200 1 200 or see hepctrust.org.uk.

Committee votes to mandate organ donor decision

<http://abclocal.go.com>

TRENTON, N.J.-February 14, 2008 -- If you ask Diane Bottino, it wasn't the hepatitis C that killed her husband last year, it was the needless waiting.

"What ultimately caused my husband to die was the shortage of organ donations," she said.

Joseph Bottino, 42, died after waiting 15 months for a liver transplant. Now his wife hopes a measure to require residents to make a decision about organ donation stops another sick person from dying the same way her husband did.

On Thursday, a New Jersey Senate committee voted to require people applying for driver's licenses and identification cards to state whether they want to be an organ donor.

The measure would also require high schools to teach about organ donation.

Howard M. Nathan, president and CEO of the Gift of Life Donor Program, said New Jersey would be the first state to impose such requirements.

"Our point is to encourage folks to have these conversations with their loved ones before they get to a hospital," said Senate President Codey, the bill sponsor. "It's designed to move the conversation from the emergency room to the living room."

About 105,000 people in the United States await organ donations, according to the United Network for Organ Sharing.

"For the first time, a state is advocating that it is the fundamental responsibility of its residents to help save another person's life," Nathan said.

While states ask license and identification applicants if they want to be an organ donor, they aren't required to answer.

Codey's bill would require applicants to answer whether they want to become an organ donor. If they decide to do so, their donor status would appear on their license and be maintained in a state registry.

If they're not ready to make a decision or uncomfortable sharing it, they would designate someone to make that decision on their behalf when the time comes.

"Let's get people talking about it at home, and many families will avoid the unnecessary heartache that is now my family's reality," said Bottino, of Haddonfield.

Sen. Joseph Vitale, the Senate health committee chairman, said the bill, which can now be considered by the full Senate, would help.

"This will make a real difference and will over time save lives," said Vitale, D-Middlesex.

Codey, D-Essex, said he hopes other states and the federal government follow New Jersey.

Senators released the bill after rejecting claims from Motor Vehicle Commission officials who argued the requirements would prove burdensome.

"This bill puts a lot of fiscal constraint on us," said Denise Coyle, the agency's chief of staff.

Kay Pittman Govito of Moorestown said organs from her son David helped save four people. David Gregory Govito died in 2003 at age 31 in California after hitting his head on pavement after being punched.

"Four people live on because of my son," Govito said, "and I do, too, because I was able to resurrect, be a mother, be a wife, be a daughter, be a sister, because my son does live on, just not in the traditional sense."

GenOdyssee Receives Notice of Allowance from U.S. Patent Office for Improved Interferon-Alpha Aimed at Hepatitis C

<http://biz.yahoo.com/>

*GenOdyssee has Received Notice of Allowance of United States Patent Application Covering its Lead HCV Interferon-alpha Product **GEA007.1**, a Natural Protein With Improved Anti-HCV Genotype 1 Activity*

PARIS, France, February 14 /PRNewswire/ -- GenOdyssee S.A., a biotechnology company dedicated to the discovery and development of improved 'next generation' blockbuster protein therapeutic products, announced today that it has received notice of allowance from the United States Patent and Trademark Office (USPTO) of its Patent Application Ndegrees 10/691,653 covering its lead anti-HCV IFN-alpha product GEA007.1 for application in the treatment of hepatitis C. GEA007.1 is a naturally occurring mutant of human **IFN alpha 17**. In preclinical studies, GEA007.1 demonstrated improved intrinsic anti-genotype 1 antiviral properties without increased toxicity at therapeutic doses used in HCV treatments, as compared to standard of care IFN-alpha 2 drugs.

"We are very happy with this notice of allowance, which represents an important milestone for us. Combined with the granting in the European Union in 2006 of our patent application covering GEA007.1, this is a proof-of-concept of the global standard of innovation set by our lead HCV program," said Jean-Louis Escary, Ph.D., CEO of GenOdyssee. Similar to the European Patent Office notice of allowance report on this product that was issued in 2006, the current USPTO notice of allowance report did not reveal any prior art references relevant to the invention constituted by GEA007.1.

A recent communication with the USPTO revealed that GenOdyssee's patent application covering a second lead IFN-alpha drug candidate, GEA009.2, to be used in cancer, is expected to be allowed in the United States in the near future. "This confirms the uniqueness of GenOdyssee's proprietary technology as well as our global leadership position in the interferon arena," said Dr. Escary. "Our technology has also proven to be uniquely applicable to other important classes of protein therapeutic drugs such as erythropoietin".

Genotype 1 HCV has in recent years become the predominant HCV genotype worldwide. It is estimated that approximately 100 million people are infected with HCV genotype 1 worldwide and that this genotype kills around 200,000 people annually from cirrhosis-related hepatocarcinoma. Genotype 1 patients have not shown improved responses to other IFN-alpha2 variants currently in clinical testing, nor have these patients responded to higher doses of standard-of-care long-lasting IFN-alpha2 drugs. Therefore, says Dr. Escary, "GenOdyssee's improved interferon-alpha variant drug for HCV genotype 1, GEA007.1, which presents no increase in toxicity at therapeutic doses used in HCV treatments, can constitute the next standard of care. GenOdyssee is developing both standard and pegylated versions of GEA007.1 and we believe this will provide a key element in meeting the proven and growing demand for better hepatitis C therapies" added Escary.

About GenOdyssee S.A.

GenOdyssee applies its proprietary population-genetics-based drug discovery approach using a DNA databank representative of more than 90% of the different ethnicities that constitute the current human population, which is screened for natural genetic variants of therapeutic proteins with superior properties. The company pioneered the vision that natural evolution has led to the generation in the current population of unpredictable mutations that confer superior or novel

therapeutic status to known important human therapeutic proteins.

GenOdyssee's technology is protected by the international patent application PCT/EP03/13965 and is the sole property of the company. An international examination report delivered by the European Patent Office stated an absence of prior art to such technology in the entire biopharmaceutical industry.

This technology has allowed GenOdyssee to identify a variety of innovative variations on existing protein drugs including cytokines, growth factors, coagulation factors, hormones and their receptors.

GenOdyssee's lead IFN alpha products are natural human proteins variants generated by natural evolution. They are therefore already proven to be functional and tolerated in man, echoing that of the marketed interferon-alpha 2a and 2b drugs from Roche and Schering-Plough that define the current standard of care.

GenOdyssee's IP portfolio is constituted of fifty-two patents and patent applications that cover both its innovative technology and therapeutic products, representing seven different patent families among which twenty patents are already granted in numerous countries worldwide including the EU and the US.

For more information about the company, please visit the company's website at <http://www.genodyssee.com>

Source: GenOdyssee SA

February 15th, 2007

Sorafenib Plus Doxorubicin May Offer Better Time to Progression Than Doxorubicin Alone in Advanced Hepatocellular Carcinoma: Presented at ICACT

<http://www.docguide.com>

By Shazia Qureshi

PARIS, FRANCE -- February 8, 2008 -- Sorafenib (**Nexavar**) plus doxorubicin appears to offer longer time to progression compared with doxorubicin monotherapy in patients with advanced hepatocellular carcinoma, according to a study reported here at the 19th International Congress on Anti-Cancer Treatment (ICACT).

In addition, patients receiving the combination have longer overall survival and progression-free survival times than do patients on doxorubicin, results of the randomised, double-blind, placebo-controlled, phase 2 study.

The findings were presented on February 7 by lead author Ghassan Abou-Alfa, MD, Medical Oncologist, Gastrointestinal Oncology Service, Memorial Sloan-Kettering Cancer Center, and Assistant Professor of Medicine, Cornell University, New York, New York.

"This trial supports the growing body of evidence of the activity of sorafenib in advanced hepatocellular carcinoma," Dr. Abou-Alfa noted.

The study included 96 patients with a median age of 65 years; 76% were men.

Enrolment criteria were advanced hepatocellular carcinoma as well as a Child-Pugh score of A (indicating a prognosis of 100% at 1 year and 85% at 2 years), no prior systemic therapy. Eastern Cooperative Oncology Group performance status was 0 or 1 (indicating they were fully active) in 91% of patients.

Patients received doxorubicin therapy intravenously at a dose of 60 mg/m² every 21 days. In addition, 47 patients were randomised to oral sorafenib at a dose of 400 mg twice daily, and 49 to placebo twice daily. Treatment duration was 18 weeks, which corresponded to 6 cycles of doxorubicin therapy. After that, patients could continue receiving sorafenib or placebo until disease progression.

Results showed a median time to progression of 8.6 months in patients receiving sorafenib and 4.8 months in patients on placebo. Median overall survival was 13.7 months in the sorafenib patients and 6.5 months in the placebo patients. Median progression-free survival was 6.9 months and 2.8 months, respectively.

One patient in the sorafenib group experienced grade 3/4 left ventricular dysfunction. Fatigue and neutropenia were the most commonly reported grade 3/4 adverse effects, and these occurred equally in both groups of patients.

"This randomised study showed encouraging time to progression and overall survival outcomes for sorafenib plus doxorubicin," Dr. Abou-Alfa concluded. "Any synergistic role between sorafenib and doxorubicin needs to be further defined."

Funding for this study was provided by Bayer Corporation.

[Presentation title: Phase II (PhII), Randomized, Double-Blind Study of Sorafenib Plus Doxorubicin (S+D) Versus Placebo Plus Doxorubicin (P+D) in Patients (pts) With Advanced Hepatocellular Carcinoma (AHCC). Abstract OR 9]

Report increases hepatitis C exposure cases to 8,896

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

Kyodo News

Opening the door to further claims for compensation by hepatitis C sufferers, the health ministry released a report Friday upping the number of people administered tainted fibrinogen blood-clotting agents in Japan to 8,896.

However, it is not known how many of them have suffered liver disease as a result.

Of the 8,896, only 3,632, or about 40 percent, have been told by medical organizations that they

were given the contaminated fibrinogen blood products to stop bleeding, mainly during delivery, ministry officials said.

The Health, Labor and Welfare Ministry worked out the figure in a nationwide survey on about 6,600 medical institutions to which the fibrinogen blood products were supplied.

Of the medical institutions, 1,622 have kept medical records, operative notes or prescription documents that could help hepatitis C sufferers seek benefits from the government and drugmakers. This represented an increase of some 1,100 from the ministry's previous survey in 2004.

This may lead to an increase in the number of people who can seek compensation from the government.

Health minister Yoichi Masuzoe on Friday criticized the ministry's 2004 survey, saying the checks should have been more thorough.

Earlier, hepatitis C sufferers who filed damages suits against the government and drugmakers estimated that only up to 1,000 people could prove they had been administered tainted blood products, based on the 2004 survey.

Hepatitis C sufferers had earlier reached a compromise agreement with the government to end their court battle under a new law that provides blanket relief measures for the sufferers.

The accord calls for providing benefits to sufferers who can prove they received contaminated blood products if the causal relationship between their hepatitis C and the products are confirmed.

Under the law, sufferers will receive compensation ranging from ¥12 million to ¥40 million each depending on the severity of their condition.

Hepatitis C tends to become chronic and can develop into cirrhosis and liver cancer.

Along with the government, three drugmakers are named in the sufferers' damages suits — Mitsubishi Tanabe Pharma Corp., its subsidiary, Benesis Corp., and Nihon Pharmaceutical Co.

Mitsubishi Tanabe is the successor to defunct blood product maker Green Cross Corp., which made the fibrinogen. Green Cross is known as causing numerous cases of AIDS in Japan by selling HIV-tainted blood products.

In mid-January, the government and sufferers signed an accord to end the legal battle.

CROI: Choice of nucleoside analogue in co-infection: tenofovir associated with better response to HCV therapy

www.aidsmap.com

Derek Thaczuk

In people with HIV/HCV co-infection, drug interactions between nucleoside analogues and ribavirin may lead to poorer responses to hepatitis C (HCV) treatment. Two poster presentations of retrospective data by Spanish study teams at the Fifteenth Conference on Retroviruses and Opportunistic Infections showed that co-infected patients who were receiving tenofovir had the best chances of sustained response to HCV therapy.

The first poster, by José Mira and team, described a retrospective multicentre study of 256 patients, all of whom started first-line HCV therapy with pegylated interferon (peg-IFN) and ribavirin while receiving ART for HIV infection. All patients were receiving a three-drug ART regimen including one protease inhibitor (PI) or one NNRTI, plus a dual-nucleoside backbone of either: abacavir and lamivudine (3TC), tenofovir and 3TC, or tenofovir and FTC.

The study group data was drawn from 256 patients in fifteen Spanish hospitals. Median age was 42, 78% were male, median baseline HCV viral load was 5.9 log₁₀ and median CD4 cell count was 473 cells/mm³.

All were treated with a combination of subcutaneous peg-IFN alpha-2a (180 µg/week) or alpha-2b (1.5 µg/kg/week) plus oral ribavirin (RBV) at 600 to 1500 mg/day. Treatment duration was 48 weeks for patients with HCV genotype 1 or 4, and 24 or 48 weeks at the treating physicians' discretion for genotypes 2 and 3. Temporary discontinuations or dose reductions of peg-IFN and/or RBV were also at the physicians' discretion. Such dose reductions were made for 10% to 12% of patients, with no significant difference between those on tenofovir or abacavir.

In an intention-to-treat analysis, significantly better responses to HCV therapy were seen with tenofovir than with abacavir. Lower SVR in patients taking abacavir was most pronounced and significant in those who received lower ribavirin doses; at higher doses, the trend remained but became statistically insignificant. SVR was as follows:

	Tenofovir + (3TC or FTC)	Abacavir + 3TC	p-value
All (n=186)	45% (n=186)	29% (n=70)	p=.02
RBV dose < 13.2 mg/kg/day	52%	20%	p=.03
RBV dose ≥ 13.2 mg/kg/day	38%	31%	p=0.4*

(*not significant)

In multivariate analysis, a tenofovir-containing regimen independently predicted SVR (adjusted odds ratio [OR], 2.6; 95% confidence interval [CI], 1.05 to 6.9; p=.03). SVR was also greater for those with HCV genotype 2 or 3 (OR, 8.9; 95% CI, 4 to 20; p<.001), baseline LDL cholesterol levels ≥100 mg/dL (OR, 3.06; 95% CI, 1.4 to 6.7; p=.004), lower baseline plasma HCV RNA load (OR, 1.85 per log₁₀; 95% CI, 1.1 to 3.1; p=.016) and undetectable baseline HIV viral load (OR, 3.5; 95% CI, 1.01 to 12.5; p=.003).

The other poster, by González-García and team, described another, larger retrospective multicentre study. This study included data on 719 patients from 35 sites who initiated first-line HCV therapy between January 2003 and November 2005. In this case, however, their

concomitant ART therapy consisted of dual NRTIs plus an NNRTI or a PI, or triple-nucleoside therapy including abacavir.

The analysis in this case compared the SVR between two groups: the 238 tenofovir-receiving patients, and the 481 not receiving tenofovir. The TDF group were taking TDF plus 3TC or FTC; the non-TDF group included those on AZT+3TC (n=265), d4T+3TC (n=164), or ABC+3TC (n=52). Patients on triple-nucleoside therapy (AZT+3TC+ABC) were counted in the AZT+3TC group (number not reported). Those receiving didanosine (ddI), or TDF in combination with either AZT, d4T or ABC, were excluded.

Baseline characteristics were similar to the first group: median age was 41 years and 75% were male. Other baseline characteristics were well-matched between the TDF and non-TDF groups except for somewhat lower CD4 cell counts (535 vs. 601 cells/mm³; p=.003), exposure to more antiretroviral regimens (7.2 vs. 5.7, p<.001), and more lipodystrophy (30.3% vs. 22.9%, p=.033) in the TDF group.

Ribavirin doses were reduced more often in those who did not receive TDF than in those that did (12.8% vs. 19.5%, p=.03), especially in those who received AZT (23.2%, p=.003)

The raw intention-to-treat (ITT) analysis found no differences in SVR between the TDF-treated and non-TDF-treated groups (45% vs. 39%, p=.12). Multivariate analysis adjusted for the five factors which predicted response in univariate analysis: HCV genotype, alcohol intake > 50 g/day, and baseline HCV viral load (<500,000 IU/mL), HIV viral load (<50 copies/mL), and AST/ALT ratio. Results from this analysis were as follows:

NRTI group	Odds ratio (OR) for SVR	95% CI	p
TDF+3TC or FTC (n=238)	1.70	1.05 to 2.77	0.03
AZT+3TC (incl. AZT+3TC+ABC) (n=265)	0.60	0.37 to 0.99	0.05
d4T+3TC (n=164)	1.09	0.65 to 1.82	0.73*
ABC+3TC (n=52)	0.80	0.32 to 2.08	0.68*

(*not significant)

Discussion

Both studies, therefore, were in agreement that tenofovir was associated with better sustained virologic responses to first-line HCV treatment. Previous reports, however, have found that poorer SVR may result in patients on abacavir-containing regimens - an issue these posters did not entirely clarify.

The Mira study, drawing on previous findings of poorer HCV response in patients taking abacavir, specifically addressed whether AZT might have had a confounding effect in this scenario. By excluding patients on AZT, Mira found that the preferential effect of tenofovir over abacavir (in the presence of 3TC or FTC) persisted.

The González-García study reached slightly different conclusions: that tenofovir was associated with improved HCV SVR, but that AZT – not abacavir – was associated with poorer tolerability and efficacy. There was not, in this study, a significantly different outcome for patients on dual-nucleoside therapy including abacavir. In this study, an unspecified number of patients on abacavir-containing triple-nucleoside therapy were grouped with the other patients on AZT, not abacavir; and change of ART was considered as treatment failure. It might have been illuminating to see the triple-nucleoside patients included in the abacavir arm for analysis.

Both studies were also retrospective analyses. Further, prospective studies may be needed to fully distinguish the impact of AZT and abacavir on pegylated interferon/ribavirin treatment for HCV.

References:

Mira JA et al. Efficacy of pegylated interferon plus ribavirin treatment in HIV/hepatitis C virus-coinfected patients receiving abacavir plus lamivudine or tenofovir plus either lamivudine or emtricitabine as nucleoside analogue backbone. Fifteenth Conference on Retroviruses and Opportunistic Infections, Boston, poster abstract 1074, 2008.

González-García J et al. The use of tenofovir plus 3TC/FTC is associated with an improved response to pegylated interferon plus ribavirin in HIV-HCV co-infected patients receiving HAART. The Gesida 50/06 study. Fifteenth Conference on Retroviruses and Opportunistic Infections, Boston, poster abstract 1076, 2008.