

# HCV ADVOCATE WEEKLY NEWS REVIEW

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

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Nov 1, 2008

### ***Schering-Plough says hepatitis C data positive***

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

BOSTON, Nov. 1 (Reuters) - Schering-Plough Corp (SGP.N: Quote, Profile, Research, Stock Buzz) said its experimental drug to treat hepatitis C is more effective in eradicating the virus in previously untreated patients than standard therapies for the serious liver disease.

Data released on Saturday at the annual meeting of the American Association for the Study of Liver Diseases in San Francisco showed that the drug, **boceprevir**, when given in combination with the standard treatments peginterferon and ribavirin, was more effective than the standard treatment alone.

The main goal of the 595-patient trial, known as SPRINT-1, was to establish the rate at which patients maintain a sustained viral response (SVR), defined as the eradication of the virus to undetectable levels, at 24 weeks following the end of treatment.

The company said that 24 weeks after a 28-week period of treatment, 56 percent of patients had no detectable virus in their system. That compared with 38 percent for those who took the standard treatment alone. Patients in the boceprevir arm received four weeks of standard therapy followed by 24 weeks of triple combination treatment.

For patients who did not receive the four-week lead-in treatment, but took the triple combination for all 28 weeks, the SVR rate was 55 percent.

Schering-Plough said the trial has not been going on long enough to show the SVR rate at 24 weeks following 48 weeks of treatment, which is the typical length of time needed for existing treatments to work.

Schering-Plough and rival Vertex Pharmaceuticals Inc (VRTX.O: Quote, Profile, Research, Stock Buzz), which is developing a competing drug called telaprevir, hope to reduce the time needed for treatment by as much as half.

At 12 weeks after the end of 48 weeks of treatment, including a four-week lead-in time, the boceprevir SVR rate was 74 percent. That compared with a rate of 66 percent for patients who took the triple combination regime for all 48 weeks, with no lead-in period. The SVR rate in the control group was 38 percent.

Fewer patients in the lead-in arms discontinued treatment due to viral breakthrough compared with those who did not have a lead-in period.

The company said the rationale for the lead-in treatment regimen is based on the fact that both peginterferon and ribavirin reach steady concentrations by week four, so patients have the new drug added at a time when the standard care drug levels have been optimized.

The most important side effects in the boceprevir arms of the trial were fatigue, anemia, nausea and headache, the company said. There was no increase in skin disorders such as rash, which has been a concern with telaprevir.

Boceprevir and telaprevir work by inhibiting an enzyme essential for the virus to replicate.

Hepatitis C is a blood-borne liver disease that can cause chronic liver disease, liver cancer and cirrhosis. It affects about 3.4 million people in the United States. (Reporting by Toni Clarke, editing by Richard Chang)

## ***Vertex Drug for Hepatitis C Shows Durable Virus-Killing Ability in Tough-to-Treat Patients***

<http://www.xconomy.com>

Luke Timmerman

More data is rolling in from Vertex Pharmaceuticals on its lead drug for hepatitis C, and it looks like the medicine is continuing to live up to its own high expectations. The Cambridge, MA-based company said today that **telaprevir**'s effect on killing the virus is remaining durable on follow-up analysis, and the drug appears to just about as good in a more convenient twice-daily pill form instead of its standard three-times-a-day dosing schedule.

The data dump came in front of a prime audience of physicians attending the American Association for the Study of Liver Disease annual meeting today in San Francisco. The results

appear to match up pretty consistently with what Vertex has reported previously, which I wrote about in this advance story.

To recap what's at stake, telaprevir is aiming to be a first-in-class protease inhibitor against hepatitis C, a chronic liver disease. If it can deliver in the final stage of clinical trials, it will change the standard of treatment for the disease. An estimated 3.2 million people in the U.S. have hepatitis C infections, and about 170 million have it worldwide. Telaprevir must be taken with a pair of standard drugs, pegylated interferon alpha and ribavirin, which cause flu-like symptoms and must be taken for almost a year. The Vertex drug is highly anticipated, though, because it has shown in earlier trials that it can almost double the cure rate for patients when added to standard therapy, and in half the time. If approved, the product could generate \$2.6 billion in U.S. sales in 2013, according to Rachel McMinn, an analyst with Cowen & Co. in San Francisco.

“These are strong and striking early results,” says Freda Lewis-Hall, Vertex's executive vice president for medicines development.

In the spirit of helping you keep all this data straight, because there's a lot of it, we're breaking this down into bite-size chunks. .

—**The '107 study.** This trial of patients who didn't respond to previous treatment, produced data from more patients who were followed over a longer period than was previously reported. Researchers found that 68 of 104 patients, or about two-thirds, who got telaprevir along with standard drugs had no evidence of the virus in their blood after four weeks. That effectiveness appeared to be long-lasting. Researchers found that 41 of 71 patients (58 percent) followed for 24 weeks still had no evidence of the virus in the blood. Importantly, telaprevir is showing that it can wipe out the virus about 43 percent of the time in the toughest patients of all to treat—those who didn't respond at all to a prior round of therapy.

The last time Vertex reported results from this trial, at a European meeting in April, it didn't have any follow-up data that extended this long, or such strong data for what are called “null responder” patients. Of course, there were side effects, though. About 8 percent of patients dropped out of the study because of adverse events, with about half of them quitting because they developed a rash, the company said.

—**The C208 study.** This trial is about convenience for patients. Telaprevir is designed to be taken three times a day in combination with standard drugs, and its ongoing final-stage clinical trials are enrolling patients on that dosing schedule. But the company also wants to know if it might be equally good in a more convenient twice-daily form. The results of this study suggest it could be. Researchers found 76 of 82 patients (93 percent) had their virus completely wiped out in the blood after three months on the usual telaprevir-containing regimen, while more than 80 percent in a comparison group did that well on a twice-daily telaprevir dose. “The question is do we continue to study twice-daily regimens based on what we see? The answer is yes,” says Lewis-Hall.

—**Prove 3.** Not a lot of news on this one. The Prove 3 study of telaprevir for patients who failed on previous therapy, first released in June, found that 60 of 115 patients (52 percent) who got the Vertex drug along with the standard drugs had no signs of the virus after about three months of

follow-up after finishing treatment, the company said. That number is consistent with what Vertex is reporting to doctors at the liver meeting. It notes that 34 of 114 patients (30 percent) in a control group taking the standard meds had undetectable amounts of virus in the blood after they were three-quarters of the way through their nearly yearlong course of treatment. The true test of what's considered a "clinical cure" is when patients have no sign of virus a full 24 weeks after they finish treatment, and that data isn't yet available for release at this meeting, Vertex says.

About 16 percent dropped out of the Prove 3 study early because of adverse events, while just four percent of patients in the control group quit, the company says. In the final analysis of the Prove 2 study, which enrolled patients who were new to treatment, about 14 percent dropped out because of adverse events, compared with half that many in the control group.

When looked at altogether, Vertex now has more than 1,000 patients who have been analyzed for the safety of its drug.

Based on my conversation with Vertex's chief commercial officer, Kurt Graves, heading into the meeting, it doesn't seem like this data will surprise physicians who have been following the telaprevir story. He sounds like he'll be keeping an eye on competitors like Schering-Plough's boceprevir and other types of antivirals in development, like polymerase inhibitors and NS5A inhibitors, which might be combined with telaprevir. We'll keep a close eye on this to see if anybody makes any big steps forward or back.

## ***Anadys Drug Found Safe in Small Study, Aims to Contend in New Class of Hepatitis C Meds***

<http://www.xconomy.com>

Luke Timmerman

Anadys Pharmaceuticals may not be first in a new class of emerging drugs for hepatitis C, but it's aiming to show this weekend it's a contender. The San Diego-based company is reporting today that its lead drug candidate was found safe at a variety of doses in a clinical trial of 48 healthy volunteers, and appears to have potential to be given as a once-daily or twice-daily pill.

San Diego-based Anadys (NASDAQ: ANDS) reported results on **ANA598** at the American Association for the Study of Liver Disease meeting today in San Francisco. The company (pronounced Uh-nad-iss), found its drug appeared to be highly potent against the virus at the second-lowest dose tested, and that no serious side effects were reported among any patients, whether they took 400 milligrams, 3000 milligrams, or anything between, researchers said at the liver meeting.

"We're comfortable predicting that we're going to have an antiviral effect," said CEO Steve Worland. "This puts our stake in the ground."

This safety data is important to Anadys. Its stock was cut in half on June 26, 2006 after one of its other candidates, ANA975, was found to cause "intense immune stimulation" in animals. That drug was scrapped a year later when another animal study confirmed the unwanted effect, which caused a partnership with the drug giant Novartis to unravel.

Now Anadys is taking a new approach with ANA598, a polymerase inhibitor drugs against hepatitis C. These drugs could be added in combination treatments with protease inhibitor drug candidates now in later stages of development from Vertex Pharmaceuticals and Schering-Plough. They're all chasing a big market opportunity, with 3.2 million people in the U.S. infected with hepatitis C, and an estimated 170 million worldwide.

The Anadys drug is going up against some tough players in its quest to develop a polymerase inhibitor for hepatitis C, namely Gilead Sciences (NASDAQ: GILD) and a partnership between Roche and Pharmasset. Those companies are further along in development than Anadys, Worland says, plus Abbott Laboratories and Pfizer are working in the field at earlier stages. They are drawn to this class of polymerase inhibitors because doctors see potential for them to add punch to protease inhibitors, since the different drugs attack different parts of the virus, Worland says.

“What people want is to use more than one antiviral in combination with each other. It's building on the HIV paradigm,” Worland says.

The data from Anadys and its competitors is being watched carefully by the bigger players in hepatitis C treatment.

Vertex's chief commercial officer, Kurt Graves, told me his company is looking at emerging polymerase inhibitors, and NS5A inhibitors, which might someday offer patients a chance to get rid of a standard combination treatment they must take, of pegylated interferon alpha and ribavirin. Those drugs must be taken for almost a year; cause serious flu-like symptoms that make them difficult to tolerate, and only cure the virus for about one-third of patients.

The Anadys data, while still at an early stage, suggests it could be used in combinations, Worland says. Anadys saw in this Phase Ia trial that patients who took an 800 milligram dose of its drug twice-daily were able to get almost five times the amount of drug needed in the bloodstream to wipe out the virus. The drug, however, wasn't given to actual hepatitis C patients. The next step, which the company announced earlier in the week, is to recruit 30 hepatitis C patients for another study that will look at the drug's safety. That study also will look at early indications of its virus-killing ability at 200 milligrams, 400 milligrams, and 800 milligrams twice a day, the company has said. Data from this trial will be available in the first quarter of 2009, Worland says.

Since it's been gaining confidence from its clinical trial results, Anadys is going to continue carrying on partnership talks with a number of companies that are interested in combining treatments, Worland says. To add some complexity to the discussions, Anadys has another drug candidate for hepatitis C, **ANA773**, which is designed to stimulate the body to produce interferon proteins. That could be used in combination with any number of antivirals, and could replace the standard pegylated interferon alpha, Worland says.

The market for hepatitis C drugs may grow to \$8 billion in 2015, according to analyst Brian McCarthy with Merriman Curhan Ford & Co., in a note to clients earlier this year. Anadys isn't saying when it thinks it get its first drug on the market, but if it can grab even a fraction of that kind of cash, then it will be on its way to becoming one of the bigger biotechs in San Diego. It's

still pretty early to handicap this race, though. "This is a complex poker game, with new cards being turned over every round," Worland says.

## **GlobeImmune Hepatitis C Therapeutic Vaccine, GI-5005, Doubles Viral Clearance and Increases RVR Rates in Phase 2 Clinical Trial**

<http://www.marketwatch.com>

*Four-Week Data Comparing GI-5005 Plus Standard of Care vs. Standard of Care to Be Presented Next Week in Late-Breaking Poster at AASLD Meeting; AASLD President Will Highlight Data at President's Press Conference*

LOUISVILLE, CO, Nov 01, 2008 (MARKET WIRE via COMTEX) -- Four-week Phase 2 clinical trial data show that **GI-5005**, GlobeImmune's hepatitis C virus (HCV) targeted molecular immunogen (**Tarmogen(R)**), doubled viral clearance overall and in all major subgroups and doubled the rapid virologic response (RVR) rate in naive patients with high viral load. The study compared GI-5005 plus standard of care (SOC) -- pegylated-interferon plus ribavirin -- versus SOC alone in patients with chronic genotype 1 hepatitis C infection.

The study data will be presented by principal investigator John G. McHutchison, M.D., of Duke University, in a late-breaking poster next week at the 59th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD). Treatment-naive patients with high viral loads at baseline ( $> 600,000$  IU/mL) saw a 2.6-fold improvement in RVR, which is defined as undetectable HCV RNA levels ( $< 25$  IU/ml) by four weeks. Treatment-naive patients with a high viral load at baseline are particularly difficult to treat to an RVR. RVR is highly predictive of whether a patient will achieve a sustained virologic response (SVR), or "cure," which is defined as undetectable HCV RNA at six months post-treatment. A significant improvement was also noted in the rate of viral reduction in the peripheral blood using viral kinetic analysis in all patients, with a 2-fold improved slope ( $0.32 \log_{10}/\text{month}$  difference,  $p=0.02$ ) for patients receiving GI-5005 in addition to SOC. Comparable magnitude of increased viral clearance in GI-5005 treated patients was noted in all patient subgroups including prior non-responders and patients with high viral load at baseline.

"These data represent early but important evidence that a patient's natural immune response can be harnessed to positively influence important virologic endpoints with the potential to impact the course of chronic HCV infection," said Dr. McHutchison. "The rational combination of novel immune approaches such as GI-5005 with IFN-based standard of care or with novel direct acting antiviral agents holds promise in terms of ultimately improving clinical outcomes, shortening the exposure to toxic therapies, or both."

David Apelian, M.D., Ph.D., GlobeImmune Chief Medical Officer, said, "These data indicate that GI-5005 can increase the rate of clearance of infected cells from the liver, something that interferon-based therapies and antivirals are not designed to do. Direct acting antivirals act primarily by inhibiting viral replication, an important step, but they have not been shown to speed the immune clearance of infected cells from the liver. Ultimately, to achieve sustained virologic response, HCV must be eradicated not just from the blood, but also the liver. GI-5005 may improve this critical part of the treatment and healing process in a way that is complementary to standard of care and the new direct acting antivirals."

An HCV-targeted cellular immune response is essential to curing a patient with hepatitis C. Twenty percent of patients infected with hepatitis C have immune responses strong enough to clear the virus on their own, without medical intervention. However, for the remaining 80 percent who go on to develop chronic infection, it takes the immune system six to twelve months to eliminate the infection, even with SOC and the best antivirals. Improving the rate of viral clearance may ultimately lead to a decrease in the time needed for therapy.

"The role of the immune response in combating hepatitis C infection is often overlooked," added Apelian. "Most of the recent development interest has been focused on new direct-acting antivirals, which inhibit viral replication. However, to improve the rate of viral clearance from the liver, it is necessary to stimulate an HCV targeted cellular immune response. We believe that the Phase 2 data to date demonstrate the potential of GI-5005 to be an important and complementary part of the treatment of hepatitis C."

The GI-5005-02 clinical trial is a randomized, multi-center, Phase 2 study evaluating 140 patients, all with genotype 1 HCV infection. In the trial, 74 percent of the patients had never received prior treatment, and the remaining 26 percent experienced prior treatment failures.

GlobeImmune's GI-5005 is a targeted molecular immunogen (Tarmogen(R)) designed to elicit an HCV-specific T-cell response. Tarmogens are whole, heat-killed recombinant *S. cerevisiae* yeast that express antigens from one or more disease-related proteins.

#### **About GlobeImmune**

GlobeImmune Inc. is a private company developing targeted molecular immunogens, Tarmogens(R), for the treatment of cancer and infectious diseases. The company's lead product candidate, GI-5005, is a Tarmogen for the treatment of chronic hepatitis C infection (HCV). GI-5005 is designed to complement both the current standard of care and emerging novel therapies for HCV. The company's lead oncology program, GI-4000, targets mutated versions of the Ras oncoprotein for the treatment of pancreas cancer as well as other cancers that contain mutated Ras, including non-small cell lung cancer and colorectal cancer.

For additional information, please visit the company's Web site at [www.globeimmune.com](http://www.globeimmune.com).

*SOURCE: GlobeImmune, Inc.*

#### ***Tibotec Presents Interim Findings for TMC435, an Investigational Genotype 1 Hepatitis C Treatment, at the AASLD Liver Meeting 2008***

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

SAN FRANCISCO, Nov 01, 2008 /PRNewswire via COMTEX/ -- Nearly 90 percent of patients achieve undetectable viral load in Phase IIa trial within 28 days of combined treatment with standard of care

New clinical data show antiviral activity of **TMC435**, an investigational protease inhibitor (PI) being developed by Tibotec BVBA for the treatment of chronic hepatitis C virus (HCV) infection. Tibotec will present findings from three TMC435 studies, including a late-breaker

poster on the proof-of-principle phase IIa trial, OPERA-1 (TMC435-C201), at the American Association for the Study of Liver Disease's (AASLD) Liver Meeting 2008 in San Francisco.

The current standard of care treatment for HCV infection, pegylated interferon (Peg-IFN) combined with ribavirin (RBV), is effective in 30 to 50 percent of patients infected with chronic genotype 1 HCV infection, the most common type in the United States.(1) The development of new therapies and strategies for treating HCV, particularly the introduction of direct antivirals, may offer patients a new option with shorter treatment duration.(2,3)

### **TMC435 Phase IIa Study Results**

In interim findings from the first 28 days of treatment for the first cohort of fifty (50) treatment naive HCV+, genotype 1, patients (once daily dose of 25 mg or 75 mg TMC435 versus placebo), both doses showed dose-dependent antiviral activity. TMC435 was administered in combination with PegIFNalpha-2a/RBV (triple therapy) for 28 days or as monotherapy for seven days and, thereafter, in combination with PegIFNalpha-2a/RBV (triple therapy) for three weeks. There were neither serious adverse events, nor grade 3 or 4 adverse events, related to TMC435 or any safety-related treatment discontinuations during this 28 day treatment period.

The most common adverse events associated with TMC435 were nausea, diarrhea, and headache. There were no clinically relevant changes in laboratory parameters, ECGs, or vital signs. Steady-state plasma trough levels of TMC435 25 mg and 75 mg represented ~10 and >30-fold excess above the HCV replicon EC50 value, respectively.

Mean reductions of HCV RNA from baseline to day seven with TMC435 alone and in triple therapy were 2.63 and 3.47 log<sub>10</sub> IU/mL, respectively, in the 25 mg arm, and 3.43 and 4.55 log<sub>10</sub> IU/mL in the 75 mg arm. In the 75 mg four-week triple therapy arm, no viral breakthrough was observed; 9/9 patients achieved HCV RNA below lower limit of quantification (<25 IU/mL) and 8/9 patients achieved undetectable HCV RNA (<10 IU/mL) at day 28 (RVR=89 percent).

"These data provide important information about an emerging new approach to treating HCV," said Professor and Chairman Michael Manns, Hannover Medical School, Germany. "The discovery and development of new treatments is critical to improving the standard of care for the millions of people living with this disease."

As a global virology leader committed to patient care, Tibotec uses innovative science and expertise to research, develop, and manufacture, drugs for medical conditions with an unmet need. The company has successfully launched two antiviral medications for the treatment of HIV and is now building a portfolio of novel antiviral therapies for HCV with the goal of becoming a prominent leader in the treatment of this infectious disease.

TMC435 was discovered through a drug discovery collaboration between Medivir and Tibotec. Tibotec has the right to develop and commercialize the compound throughout the world, excluding the Nordic countries. In addition to TMC435, Tibotec has another PI in phase III development for the treatment of chronic HCV infection.

"Tibotec is committed to evaluating the safety and efficacy of TMC435 in clinical studies to determine its potential use in people with HCV," said Roger Pomerantz, M.D., president of

Tibotec Research and Development. "This is an important step in our mission of addressing treatment challenges of infectious diseases, including HCV, HIV and tuberculosis."

### **About the Phase IIa Study**

Investigators in five European countries assessed the antiviral activity, safety, and pharmacokinetics of two once-daily regimens of TMC435 (25 mg or 75 mg TMC435 versus placebo) in fifty HCV genotype 1 treatment-naïve patients in an ongoing double-blind, placebo-controlled phase IIa trial. Patients were randomized to receive either seven days of monotherapy with TMC435 or placebo followed by 21 days of triple therapy with TMC435 or placebo, plus PegIFNalpha-2a (180 mcg once weekly) and RBV (1000-1200 mg daily); or, 28 days of triple therapy with TMC435 or placebo, plus PegIFNalpha-2a and RBV. After day 28, patients continue on PegIFNalpha-2a/RBV alone for a total of 24 or 48 weeks at the discretion of the investigator.

TMC435 data from other studies will also be presented at the AASLD Liver Meeting.

*SOURCE Tibotec BVBA*

### ***New Study Shows that PEGASYS(R) Regimen Provides Higher Sustained Virological Response Rates for Hepatitis C Patients***

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

SAN FRANCISCO, Calif., Nov 01, 2008 /PRNewswire via COMTEX/ -- - Higher Sustained Virological Response Rates Recognized as Marker of Treatment Success –

A new, independently-conducted study being presented at the 59th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) shows that PEGASYS(R) (peginterferon alfa-2a) treatment regimens result in higher sustained virological response (SVR) rates for hepatitis C patients as compared to regimens with another pegylated interferon.(1) Comparing Today's Standard Treatment Regimens: The Milan Safety Tolerability Study

The Milan Safety Tolerability Study (MIST) randomly assigned 431 patients to receive PEGASYS or PegIntron™, both in combination with ribavirin. In the PEGASYS group, the daily ribavirin dose for genotype 1 and 4 patients was 1000-1200 mg based on weight, while patients with genotype 2 or 3 received a fixed dose of ribavirin (800 mg). In the PegIntron group, ribavirin doses ranged from 800 mg to 1400 mg based on a patient's weight in all genotypes. The primary endpoint was to compare the safety and tolerability. The secondary endpoint was to compare efficacy.

Professor Colombo, Head of the 1st Division of Gastroenterology and A.M. Migliavacca Center for Liver Disease at the University of Milan, and colleagues will present the results of a study, which found significantly higher SVR rates in patients treated with PEGASYS/ribavirin as compared to those treated with peginterferon alfa-2b (PegIntron)/ribavirin (66 percent vs. 54 percent, p=0.02). The difference was sustained in patients with the most difficult to treat forms of the virus, those infected with genotypes 1 or 4 (48 percent vs. 32 percent, p=0.02). The two regimens showed a similar safety and tolerability profile, with similar rates of serious adverse events (2 percent in both arms) and drop outs for side effects (7 percent vs. 6 percent).

"Our study combines the rigor of a randomized, controlled trial with the general applicability of a 'real-world' study, since it included all patients at our clinic who initiated hepatitis C treatment and met basic eligibility criteria," said Professor Colombo. "The results from this study prove that treatment success rates in the real world can be comparable to those achieved in clinical trials. The study also demonstrates that PEGASYS regimens enable significantly more patients to achieve a SVR."

PEGASYS has demonstrated efficacy in a broad range of patient types, even those with poor prognostic factors.

*SOURCE Roche*

**Nov 2, 2008**

## ***New Data Suggest Long-Term Treatment with BARACLUDE(R) (entecavir) May Reduce Liver Damage Caused by Chronic Hepatitis B***

<http://www.centredaily.com>

*Long-term cohorts evaluated for liver histology, including fibrosis, and viral load reduction*

SAN FRANCISCO — Bristol-Myers Squibb Company (NYSE:BMJ) today announced data from two separate cohort evaluations, in which long-term treatment with BARACLUDE(R) (entecavir) was associated with improved liver histology, including improvement in fibrosis, in chronic hepatitis B patients. The histology data were presented today at the 59th Annual Meeting of the American Association for the Study of Liver Diseases.

New long-term histology results were presented from a cohort of 57 nucleoside-naïve patients from rollover study ETV-901. ETV-901 provided long-term treatment with BARACLUDE 1 mg for patients who completed phase 2-3 studies. Patients followed in this cohort received BARACLUDE for a median of six years across the studies (ETV-022, -027 and -901) and had evaluable baseline and long-term liver biopsies. Of the 57 patients, 96 percent (55/57) experienced improvement in liver histology (improvement in how the liver tissue looks under a microscope). Improvement in liver histology was defined as greater than or equal to a two-point decrease in Knodell necroinflammatory score and no worsening of Knodell fibrosis score. Additionally, 88 percent of patients (50/57) experienced a reduction in liver fibrosis, defined as improvement in Ishak fibrosis score (greater than or equal to a one-point decrease). Fibrosis occurs when excessive fibrous connective tissue builds up in the liver in response to chronic inflammation, which can be caused by chronic hepatitis B infection.

Control of viral replication is an important goal of chronic hepatitis B treatment. At the time of the ETV-901 long-term biopsy, 100 percent of subjects with evaluable liver biopsies (57/57) had undetectable viral load (HBV DNA less than 300 copies/mL by polymerase chain reaction (PCR)).

Histology results were also presented from the open-label rollover study ETV-060, which evaluated Japanese patients with chronic hepatitis B. This cohort included 37 treatment-naïve patients and 27 patients resistant to treatment with lamivudine from two Phase 2 studies (ETV-053, ETV-052) who had liver biopsies after receiving at least three years of treatment with

BARACLUDE(R). Of these 64 patients, 100 percent (37/37) of treatment-naive patients and 89 percent (23/26(\*)) of lamivudine-refractory patients experienced improvement in liver histology (measured by a greater than or equal to a two-point decrease in Knodell necroinflammatory score), and 47 percent (17/36(+)) of treatment-naive and 32 percent (8/25(++)) of lamivudine-refractory patients experienced an improvement in liver fibrosis (greater than or equal to a one-point decrease in Knodell fibrosis score).

"These data suggest that long-term treatment with BARACLUDE has the potential to stop liver damage and may even improve liver fibrosis caused by chronic hepatitis B infection," said Professor Yun-Fan Liaw, lead investigator for the Long-term Histology Cohort (subset of ETV-901), from Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taipei, Taiwan. "The ability to provide effective long-term treatment with a potent antiviral with minimal resistance represents a positive step forward."

### **About the ETV-901 Analysis**

ETV-901 is a long-term rollover study for patients who previously completed phase 2-3 entecavir studies. The long-term histology cohort included 57 nucleoside-naive patients who received a minimum of 3 years of cumulative therapy with BARACLUDE from the start of studies ETV-022 or -027(1,2) (BARACLUDE 0.5 mg) to the time of their last observed biopsy in ETV-901 (BARACLUDE 1 mg), and had adequate baseline and long-term liver biopsies. These patients were treated with BARACLUDE for a median of six years. The co-primary long term histology endpoints were the proportion of patients with histologic improvement (defined as greater than or equal to a two-point decrease in Knodell necroinflammatory score and no worsening of Knodell fibrosis score) and the proportion of patients with improvement in Ishak fibrosis score (greater than or equal to a one-point decrease), both compared to baseline.

*Results of patients in ETV-901 who agreed to undergo long-term liver biopsies (median of 6 years of treatment)*

- 96% of patients had improvement in liver histology at long-term liver biopsy - an increase from 73% at week 48.
- The proportion of patients with improvement in Ishak fibrosis score increased from 32% at 48 weeks to 88% at long-term liver biopsy.
- Of the 43 patients with a baseline fibrosis score of greater than or equal to 2, 58% had a 2-point or more decrease in Ishak fibrosis score.
- 100% of patients achieved undetectable viral load (HBV DNA less than 300 copies/mL by PCR).
- Grade 3-4 adverse event(s) were reported in 20% of patients, and serious adverse event(s) were reported in 25%. The most common adverse events were upper respiratory tract infection (23%); headache (16%); nasopharyngitis, an inflammation of the nose and throat (16%); ALT increase, an increase in the production of the liver enzyme ALT, which may indicate inflammation of the liver or liver damage (14%); abdominal pain (13%); influenza (13%); back pain (12%); pyrexia-fever (12%); arthralgia-joint pain (10%); cough (10%); hypertension (10%); insomnia (10%); and pharyngolaryngeal pain - throat pain (10%).

### **About the ETV-060 Analysis**

ETV-060 was an open-label rollover study of Japanese chronic hepatitis B patients, including 66 treatment-naive patients who completed 52 weeks of treatment with BARACLUDE(R) 0.1 mg or

0.5 mg in study ETV-053, and 82 lamivudine-refractory patients who completed 52 weeks of treatment with BARACLUDE 0.5 mg or 1 mg in study ETV-052. In the ETV-060 rollover study, patients continued treatment with BARACLUDE at 0.5 mg (treatment-naïve patients) or 1 mg (lamivudine-refractory patients). The current analysis evaluated the long-term histologic results for patients who had liver biopsies after receiving at least three years of continuous treatment with BARACLUDE (37 patients from ETV-053 and 27 patients from ETV-052). Histologic improvement (greater than or equal to a two-point decrease in Knodell necroinflammatory score) and improvement in Knodell fibrosis score (greater than or equal to a one-point decrease) were evaluated for patients with biopsies at baseline, Week 48 and Week 148.

*Results of patients in ETV-060 who agreed to undergo long-term liver biopsies (at least 3 years of treatment)*

- Among both treatment-naïve and lamivudine-refractory CHB patients, liver histology improved after three years of continuous BARACLUDE(R) treatment. At week 148, 100% (37/37) of treatment-naïve patients and 89% (23/26(\*)) of lamivudine-refractory patients experienced improvement in Knodell necroinflammatory score, and 47% (17/36(+)) of treatment-naïve and 32% (8/25(++)) of lamivudine-refractory patients experienced an improvement in liver fibrosis as measured by the Knodell fibrosis score.
- At week 148, 95% (35/37) of treatment-naïve patients and 56% (15/27) of lamivudine-refractory patients had HBV DNA less than 400 copies/mL.
- Safety results for this cohort analysis were not reported at this conference. Please see the following Important Safety Information for BARACLUDE, including boxed WARNINGS in bold.

**Nov 3, 2008**

## ***Top court weighs drugmaker liability for harm***

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

By Lisa Richwine

WASHINGTON (Reuters) - Pharmaceutical companies should not be liable for harm from medicines which carry warnings approved by federal regulators, lawyers for drugmaker Wyeth and the Bush administration told the U.S. Supreme Court on Monday.

The court is considering a case that could sharply limit lawsuits against drugmakers if the justices decided Food and Drug Administration approval shielded companies from liability claims under state law.

Wyeth is battling a guitarist, Diana Levine, who lost part of an arm after she was improperly injected with an anti-nausea drug made by the company as part of treatment for a migraine.

The prescribing instructions for the drug, Phenergan, "plainly comprehended and warned about the specific risks" of giving the drug in the way Levine received it, attorney Seth Waxman, arguing for Wyeth, told the court.

The company was required to use the FDA-approved warnings and could not have changed them without the agency's permission, Waxman said.

But Levine's lawyer said Wyeth knew the injection method used for Levine was dangerous and the company should have put a stronger warning on the drug.

"These kinds of risks come to light frequently with drugs that are on the market, and the need to revise these labels is the duty of the manufacturer," attorney David Frederick said.

Justice Antonin Scalia appeared to back Wyeth's position.

"If you're telling me the FDA acted irresponsibly, then sue the FDA," Scalia said. But holding the company liable could lead to manufacturers overwarning about beneficial drugs just to avoid lawsuits, he said.

"It would not promote public safety if you believe that the name of this game is balancing benefits and costs," Scalia said.

The justices are weighing whether FDA approval preempts state laws and protects companies from legal damages. In Levine's case, a Vermont jury awarded her \$7 million.

Federal preemption has been a goal of the pharmaceutical industry for years and has been supported by the Republican George W. Bush administration. The court's ruling in the Wyeth case also could affect millions of other businesses, the U.S. Chamber of Commerce has said.

Justice Ruth Bader Ginsburg seemed concerned that the FDA does not always make the right decision about whether a medicine is too dangerous or has proper warnings, a position argued by Levine's lawyers.

"Considering the huge number of drugs, is the FDA really monitoring every one of these?" Ginsburg asked.

With Phenergan, "the risk of gangrene and amputation is there. No matter what benefit there was, how could the benefit outweigh that substantial risk?" she added.

A decision is expected by the end of June.

The Supreme Court ruled in favor of federal preemption earlier this year. In February, the justices sided 8-1 with medical device maker Medtronic Inc after it was sued by a man harmed by a catheter during an artery-clearing procedure.

If the court ruled strongly in favor of preemption again, Democrats in Congress have pledged they would push legislation to preserve a patient's right to sue under state law.

The pending case is Wyeth v. Levine.

(Reporting by Lisa Richwine, editing by Gerald E. McCormick)

### ***Vertex Again Key Player at Hep C Meeting***

<http://www.thestreet.com>

Adam Feuerstein

SAN FRANCISCO -- Every six months, hepatitis C researchers from around the world gather to discuss new ways of combating the serious liver disease. In recent years, these biannual confabs have largely revolved around the development of a new, more potent class of drug that promises to bring cures to a larger percentage of hepatitis C patients than ever before.

Like previous meetings, the one that kicked off over the weekend here will have scientists (and the Wall Street investors and analysts who follow their work closely) talking a lot about Vertex Pharmaceuticals'(VRTX Quote - Cramer on VRTX - Stock Picks) drug telaprevir.

Data being presented will show once again telaprevir's impressive ability to directly interfere with and eliminate the virus that causes hepatitis C in patients who have failed previous treatments and in those who are being treated for the first time.

Competitors to Vertex are here, too. Schering-Plough(SGP Quote - Cramer on SGP - Stock Picks) will present data on the ability of its experimental drug boceprevir to eliminate the hepatitis C virus in previously untreated patients. Companies with drugs in less advanced clinical trials, including Pharmasset(VRUS Quote - Cramer on VRUS - Stock Picks), InterMune(ITMN Quote - Cramer on ITMN - Stock Picks), Boehringer Ingelheim, Johnson & Johnson(JNJ Quote - Cramer on JNJ - Stock Picks), Merck(MRK Quote - Cramer on MRK - Stock Picks) and Pfizer(PFE Quote - Cramer on PFE - Stock Picks), also will be presenting new or updated data.

For many biotech investors, Vertex remains a central focus of these hepatitis C meetings because the company is in the midst of conducting two large phase III studies of telaprevir, with the first results expected in the first half of 2010.

Vertex intends telaprevir to become the first new hepatitis C drug approved in years, and one that will dramatically increase the cure rate for the disease, and do so in half the time of currently approved drugs. If the plan succeeds, Vertex will grab a large share of a multi-billion dollar commercial market opportunity.

There are no sure things in drug development, which is why the value of Vertex shares swing rather wildly, especially as new data is unveiled and questions -- new and old -- are raised at these gatherings of hepatitis C researchers.

Is telaprevir the best of this new crop of hepatitis C drugs? Will Schering-Plough catch up? Are second-generation drugs already in development more potent and more convenient than telaprevir? And if so, does that leave Vertex vulnerable?

Much of the most important data at this year's annual meeting of the American Association for the Study of Liver Disease will be presented Monday and Tuesday. However, the veil on some of this data has been lifted already. Here's a recap of what's available so far:

**Vertex:**

Telaprevir stands apart from other experimental hepatitis C drugs, including Schering-Plough's boceprevir, because it appears capable of curing the disease in large numbers of patients who have failed previous treatments.

A phase II study known as PROVE 3 showed that 52% of patients treated with telaprevir had undetectable levels of virus in their systems 12 weeks after treatment was stopped, according to interim data from the study being presented at the meeting. Vertex had previously announced some of these results last June.

Patients were enrolled in PROVE 3 if they had failed previous treatment with 48 weeks of pegylated interferon and ribavirin, the current standard hepatitis C therapy. These difficult-to-cure patients were then retreated with 12 weeks of telaprevir plus interferon and ribavirin, followed by another 12 weeks of interferon and ribavirin alone for a total of 24 weeks of therapy.

Breaking down the 52% overall result further, 73% of patients who had relapsed after receiving the standard treatment were able to drop their viral loads to undetectable levels, while 41% of patients who had not responded at all to previous treatment likewise achieved undetectable viral loads.

PROVE 3 also used as a control patients who were retreated a second time with the standard interferon and ribavirin. So far, just 30% of these patients have undetectable levels of virus after 36 of a planned 48 weeks of retreatment. Final data on these control patients is not ready, but far fewer are likely to reach undetectable viral loads in the observation period following treatment, based on historical data.

In a previous phase II study known as PROVE 2, which enrolled treatment-naive hepatitis C patients, telaprevir helped 69% of patients reach undetectable viral loads 24 weeks after treatment. By comparison, 46% of patients treated with interferon and ribavirin alone saw the level of virus fall below undetectable levels.

The telaprevir regimen used in PROVE 2 was the same as that used in PROVE 3 -- 12 weeks of telaprevir plus interferon and ribavirin followed by another 12 weeks of interferon and ribavirin alone.

In all previous and ongoing clinical trials, patients take telaprevir every eight hours, or three times a day. For competitive reasons, Vertex would like twice-daily telaprevir. Interim data to be presented at the meeting suggests twice-daily telaprevir is possible and could be better than standard therapy. However, three-times-a day telaprevir still appears to be the most potent dosing schedule.

### **Schering-Plough**

Schering's drug boceprevir is posting equivalent cure rates to that of telaprevir in treatment-naive patients, although the most effective treatment cycle is twice as long.

According to results from the phase II SPRINT-1 study released here, 74% of patients on a 48-week boceprevir regimen saw their viral loads fall below the level of detection 12 weeks following the cessation of treatment.

These patients began treatment with four weeks of interferon and ribavirin (a lead-in period) followed by 36 weeks of boceprevir in combination with interferon and ribavirin.

For patients without the four-week lead in, 66% saw their virus fall below detectable levels.

Using a shorter, 28-week boceprevir regimen, 55% and 56% of patients achieved undetectable viral loads with no lead in treatment, or a lead-in treatment, respectively.

Schering-Plough is currently conducting two phase III studies of boceprevir in treatment-naive and treatment-resistant patients.

### **Pharmasset**

Pharmasset's drug R7128 hasn't been as broadly tested as those from Vertex and Schering-Plough, but the data generated so far has shown the drug to be very effective at tamping down the hepatitis C virus.

The biggest question mark hanging over the drug to date is toxicity. At an investor event Sunday, Pharmasset officials for the first time discussed in some detail the emergence of kidney toxicity seen in a safety study in monkeys.

According to Pharmasset, the monkey kidney toxicity is reversible and did not cause permanent damage. More importantly, no such problem has been observed in the short human studies of R7128 conducted to date.

Pharmasset is conducting a longer, six-month safety test of R7128 in monkeys, but at this point the company doesn't believe that the Food and Drug Administration will stop further human studies from starting in the first quarter of next year.

Still, judging by the volume of questions from investors at Sunday's meeting that began with the words, "I'd like to get back to those monkey studies ..." the issue isn't one that Wall Street is ready to put entirely to rest.

Pharmasset is developing R7128 with partner Roche, which just last week was forced to halt development of a rival hepatitis C drug derived from its own laboratories because of unacceptable safety problems.

This Roche setback upped the value of R7128. If the drug's safety can be verified, Pharmasset will be a hepatitis C company to watch.

### ***A Broad Spectrum Of Liver Disease Accurately Identified By Mayo Clinic's New Imaging Technology***

<http://www.medicalnewstoday.com>

A new study shows that an imaging technology developed by Mayo Clinic researchers can identify liver fibrosis with high accuracy and help eliminate the need for liver biopsies. Liver fibrosis is a common condition that can lead to incurable cirrhosis if not treated in time.

The technology, called **magnetic resonance elastography (MRE)**, produces color-coded images known as elastograms that indicate how internal organs, muscles and tissues would feel to the touch. Red is the stiffest; purple, the softest. Other imaging techniques do not provide this information.

"Knowing the liver's elasticity or stiffness is invaluable in diagnosing liver disease," says Jayant Talwalkar, M.D., M.P.H., a Mayo Clinic hepatologist and co-investigator on the study. "A healthy liver is very soft, while a liver with early disease begins to stiffen. A liver with cirrhosis, advanced liver disease, can be rock hard."

The study, which included 113 patients, was presented Nov. 3 at The Liver Meeting, an annual gathering of the American Association for the Study of Liver Disease, in San Francisco. Study participants had undergone liver biopsy in the year preceding the study and had a wide variety of liver diseases, including nonalcoholic and alcoholic fatty liver disease, hepatitis C, hepatitis B, autoimmune hepatitis, primary biliary cirrhosis and primary sclerosing cholangitis. Patients ranged in age from 19 to 78, and their body weight ranged from normal to severely obese.

"Results showed that elastography was highly accurate in detecting moderate-to-severe hepatic fibrosis even with the variety in age, types of liver disease and body size," says Dr. Talwalkar. Among the study's findings:

The detection of cirrhosis by MRE when compared to liver biopsy results was 88 percent accurate.

Patients with nonalcoholic fatty liver disease and no significant inflammation or fibrosis were identified with 97 percent accuracy.

"Using MRE, we can confidently avoid liver biopsies for patients with no evidence of advanced fibrosis, as well as for patients with cirrhosis," says Dr. Talwalkar.

Liver biopsies, conducted by extracting tissue samples with a needle, can underestimate the degree of hepatic fibrosis about 20 to 30 percent of the time because of the patchy distribution of fibrosis that occurs in the liver. Another drawback is that since liver biopsy is invasive, patients may be reluctant to have a biopsy performed and sometimes delay the procedure when liver disease is first suspected, says Dr. Talwalkar.

"Our goal in hepatology is to be able to diagnose liver disease early so that novel as well as established therapies can be provided to our patients," says Dr. Talwalkar. Treatment and lifestyle changes can help stop the progression of hepatic fibrosis to liver cirrhosis and liver failure, which would eventually require a liver transplant.

The incidence and prevalence of chronic liver disease is increasing in the United States. Nonalcoholic fatty liver disease has become the most common liver disease and is linked to the growing numbers of patients with obesity and diabetes. The number of patients seeking medical care for hepatitis C is also increasing. This disease, spread by coming into contact with blood contaminated by the virus, slowly damages the liver over decades.

MRE research began at Mayo Clinic about 10 years ago. The technology measures low-frequency acoustic waves transmitted into the abdomen. The wave motions measured are miniscule, 0.01 of the width of a human hair.

The noninvasive procedure takes seconds to conduct. Mayo Clinic is already using MRE to diagnose patients with liver conditions. Research is under way to study how MRE might aid in the diagnosis of Alzheimer's disease and some cancers.

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

*Also involved in the study were Mayo Clinic researchers John Gross, M.D.; Meng Yin, Ph.D.; James Glockner, M.D.; Naoki Takahashi, M.D.; Michael Charlton, M.D.; Patrick Kamath, M.D.; and Richard Ehman, M.D.*

*Source: Amy Tieder  
Mayo Clinic*

## **ZymoGenetics Presents Positive Interim Phase 1b Results in Hepatitis C**

<http://biz.yahoo.com>

*- Significant Viral Load Reduction and Encouraging Tolerability With PEG-Interferon lambda -*

SEATTLE--(BUSINESS WIRE)--ZymoGenetics, Inc. (NASDAQ:ZGEN - News) today reported that PEG-Interferon lambda showed a meaningful reduction in the amount of Hepatitis C Virus (HCV) and was well tolerated in patients with relapsed HCV in an ongoing Phase 1b clinical trial. Anti-viral activity was observed at all dose levels tested. The six patients treated once a week with 1.5 mcg/kg of PEG-Interferon lambda had a mean maximum decrease of 3.6 logs in viral load at Day 29. Treatment had minimal side effects and no hematologic toxicity. Results from 18 patients, or 3 cohorts with 6 patients each, were presented at the American Association for the Study of Liver Diseases (AASLD) annual meeting.

“PEG-Interferon lambda has become one of our company’s key assets,” said Nicole Onetto, M.D., Senior Vice President and Chief Medical Officer of ZymoGenetics. “Based on these early results, we’re encouraged by the potential for PEG-Interferon lambda to become an effective treatment with improved tolerability for treating patients with Hepatitis C. We’ve accelerated the timeline for the second part of the study, where the combination of PEG-Interferon lambda and ribavirin will be investigated.”

The Phase 1b clinical trial is evaluating the safety and anti-viral activity of PEG-Interferon lambda in genotype 1 HCV patients with relapsed disease. To date, in the single agent part of the study, PEG-Interferon lambda has been administered subcutaneously either with a weekly or biweekly schedule at doses of 1.5 mcg/kg or 3.0 mcg/kg for four weeks.

Anti-viral activity was seen in all cohorts, with the best anti-viral effect documented at 1.5 mcg/kg given weekly. All 6 patients treated in this cohort showed a 2 log or greater decrease in viral load at Day 29, with 4 of these patients having less than 1,000 HCV RNA copies at the end of treatment.

PEG-Interferon lambda was well tolerated at all dose levels, with no discontinuations due to toxicity, no treatment-related fever, no signs of hematological toxicity and no meaningful

changes in hematological parameters. Adverse events were all Grade 1 or 2. Most common adverse events were fatigue and myalgia, which were observed in only 3 patients. Primary safety findings consist of asymptomatic, reversible and mild increases in liver enzymes in some patients.

### **Presentation**

The AASLD presentation is available on the ZymoGenetics website at: [www.zymogenetics.com](http://www.zymogenetics.com).

### **PEG-Interferon lambda**

The native human protein Interferon lambda is generated by the immune system in response to viral infection. Interferon lambda mediates anti-viral activity through a receptor that is distinct from that used by Interferon alpha and is present on fewer cell types within the tissues of the body. Receptors for Interferon lambda are present on several important sites of viral infection, most notably cells of the lung and liver. Recombinant PEG-Interferon lambda, a novel, pegylated Type III interferon, has shown in vitro anti-viral activity against several viruses, including HCV. A Phase 1a healthy volunteer, single dose study showed dose-dependent pharmacokinetics, evidence of biological activity (starting at 1.5 mcg/kg) and that PEG-Interferon lambda was well tolerated at pharmacologically active doses with no fever, flu-like symptoms or hematological effects. ZymoGenetics holds worldwide rights to PEG-Interferon lambda.

### **About ZymoGenetics**

ZymoGenetics discovers and develops novel protein therapeutics that are based on the company's research and biological insights into key disease pathways. The Company developed and markets RECOTHROM® Thrombin, topical (Recombinant). Other product candidates span a wide array of clinical opportunities that include cancer, autoimmune and viral diseases. ZymoGenetics intends to commercialize product candidates through internal development, collaborations with partners, and out-licensing of patents from its extensive patent portfolio. For further information, visit [www.zymogenetics.com](http://www.zymogenetics.com).

**Nov 4, 2008**

### ***Investigators at University of Modena zero in on hepatitis C virus therapy***

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

A report, 'Safety of anti-tumor necrosis factor-alpha therapy in patients with rheumatoid arthritis and chronic hepatitis C virus infection,' is newly published data in *Journal of Rheumatology*. "The prevalence of concurrent rheumatoid arthritis (RA) and hepatitis C virus (HCV) infection is probably underestimated because of the increasing spread of this virus worldwide, especially in developing countries. In these patients, anti-tumor necrosis factor-alpha (anti-TNF-alpha) therapy may aggravate hepatitis and increase viremia," scientists writing in the *Journal of Rheumatology* report.

"We evaluated the safety of these treatments, which remain controversial. Thirty-one HCV-positive patients (23 women, 8 men, mean age 59+/-13 yrs, mean disease duration 13+/-11.5 SD yrs) with active RA [Disease Activity Score 28 (DAS28) >3.2] unresponsive to conventional therapies were treated with TNF-alpha blockers (infliximab 11, etanercept 17, adalimumab 3) at standard dosages. Safety and efficacy were evaluated at the third month of treatment and at the

patient's last observation. A significant clinical-serological improvement was recorded at the 3-month reevaluation. Mean values of patients assessment of general health on visual analog scale (range 0.100) decreased from 69+/-29 (SD) to 35+/-27 (p <0.0001), Ritchie index from 21.6+/-13.9 to 10.1+/-3.7 (p <0.0001), erythrocyte sedimentation rate from 36+/-25 to 28+/-22 mm/h (p=0.04), and DAS28 from 5.2+/-1.6 to 2.78+/-1.3 (p <0.0001); a DAS28 <2.6 was recorded in 15/31 (48%) patients. At the last observation 19 patients (61%) continued TNF-alpha blockers, and the observed benefits persisted after 22+/-11 months of followup. Mean values of transaminases (ALT) and HCV viral load showed no significant variations; TNF-alpha blockers were discontinued in only one patient because of persistently elevated ALT not correlated to the variations of HCV viremia; this latter increased significantly ( $\geq 2 \log_{10}$ ) in 4 cases. Previous observations had suggested the safety of TNF-alpha blockers for treatment of RA in patients with concurrent HCV infection," wrote C. Ferri and colleagues, University of Modena.

The researchers concluded: "Given the clinical-therapeutic implications, our results support the safety of TNF-alpha blockers in patients with HCV, provided there is close monitoring of clinical and virological data (mainly ALT and HCV viremia)."

Ferri and colleagues published their study in the *Journal of Rheumatology* (Safety of anti-tumor necrosis factor-alpha therapy in patients with rheumatoid arthritis and chronic hepatitis C virus infection. *Journal of Rheumatology*, 2008;35(10):1944-9).

## **Progenics Selects Small-Molecule Hepatitis C Drug Candidate for Clinical Development**

<http://www.tradingmarkets.com>

SAN FRANCISCO & TARRYTOWN, N.Y., Nov 04, 2008 (BUSINESS WIRE) -- PGNX | Quote | Chart | News | PowerRating -- Progenics Pharmaceuticals, Inc. (Nasdaq: PGNX | Quote | Chart | News | PowerRating) today announced the selection of a proprietary small-molecule drug candidate, designated PRO 206, for clinical development as a treatment of hepatitis C virus (HCV) infection. Pre-clinical results supporting the development of PRO 206 were presented today at the annual meeting of the American Association for the Study of Liver Diseases (AASLD) in San Francisco. PRO 206 is an orally available viral-entry inhibitor, designed to prevent HCV from entering and infecting healthy liver cells.

PRO 206 represents an innovative treatment strategy as it specifically blocks the hepatitis C virus. HCV currently is treated with interferon in combination with ribavirin, non-specific antiviral agents that are associated with significant side effects and failure rates. Targeted antiviral agents are widely viewed to be a promising approach to improving treatment of HCV infection.

"The development of specifically targeted antiviral therapy for HCV (STAT-C) has the potential to transform treatment of this disease," said Ira M. Jacobson, M.D., Chief of the Division of Gastroenterology and Hepatology and Medical Director of the Center for the Study of Hepatitis C at the Joan and Sanford I. Weill Medical College of Cornell University. "Inhibiting viral entry is a proven approach for treating other viral diseases, and I look forward to seeing this strategy explored in HCV infection."

### **PRO 206: Summary of results**

PRO 206 belongs to a class of novel small-molecule drug candidates that were discovered and developed by Progenics scientists as potent and selective inhibitors of HCV entry. The results of laboratory and animal studies of PRO 206 were described in a poster presentation at AASLD. In each of two well-established in vitro models of HCV entry and replication, PRO 206 demonstrated potent inhibitory activity at concentrations that had no measurable effect on cell viability or entry of unrelated viruses. PRO 206 also demonstrated high oral bioavailability and a prolonged pharmacokinetic half-life in animals. The antiviral and pharmacokinetic properties observed for PRO 206 suggest the potential for once-daily dosing in humans. A copy of the AASLD poster can be accessed via the following link: [http://www.progenics.com/sci\\_cal.cfm](http://www.progenics.com/sci_cal.cfm).

"PRO 206 was discovered at Progenics and reflects the outstanding efforts of our discovery scientists," said William C. Olson, Ph.D., Senior Vice President, Research and Development, Progenics Pharmaceuticals, Inc. "Our HCV entry program leverages our expertise in the discovery and development of HIV entry inhibitors such as PRO 140, which is currently in phase 2 clinical trials. We look forward to completing the IND-enabling studies in 2009 in preparation for phase 1 clinical trials."

For more information about Progenics Pharmaceuticals, Inc., please visit [www.progenics.com](http://www.progenics.com).

*SOURCE: Progenics Pharmaceuticals, Inc.*

### ***Working with U.S. Department of Defense, Canopus BioPharma Announces Phase II Human Clinical Trial for Innovative Hepatitis C Drug, CB5300***

<http://www.marketwatch.com>

*New Treatment Shows Greater Therapeutic Efficacy Than Interferon Alpha*

LOS ANGELES, Nov 04, 2008 (BUSINESS WIRE) -- Canopus BioPharma, Inc. (CBIA:CBIA CBIA,); ([www.canopusbiopharma.com](http://www.canopusbiopharma.com)) today announced that permission has been granted by the U.S. Department of Defense to initiate a Hepatitis C efficacy and safety human clinical Phase II trial, testing the patented antiviral drug **CB5300**.

The 15-patient, Phase II clinical trial will be conducted at Brooke Army Medical Center in Texas and will be directed by Lt. Colonel. Stephen Harrison, Ph.D. The study will involve administering CB5300 orally to individuals with chronic Hepatitis C who have not previously undergone drug treatment or therapy for the disease. CB5300 will be administered as a monotherapy, with detailed monitoring and reporting of viral load and liver enzymes.

"We are excited to begin the clinical trial with our partners at the U.S. Department of Defense," said Patrick T. Prendergast, Chairman and CEO, Canopus BioPharma. "Our pre-clinical data shows very promising results, and we expect this clinical trial will confirm that taking CB5300 translates into a greater quality of life for those living with Hepatitis C."

CB5300 represents a unique family of molecules that are non-toxic in nature and are registered with the FDA as having GRAS (Generally Regarded As Safe) status. The molecules, which have potent antiviral properties against a wide range of viruses, were first discovered to be antiviral by Canopus BioPharma a number of years ago. The company successfully refined, isolated, and patented the most active molecules as CB5300.

Prior to developing the Phase II trial, Canopus BioPharma tested CB5300 at the Southern Research Institute in Alabama against the BVDV Hepatitis (HCV) assay model--the industry accepted standard laboratory test for anti-HCV activity. The selected CB5300 molecules displayed specific antiviral activity against BVDV and overall assay performance was validated by the positive control compound, Recombinant Interferon Alpha, which exhibited the expected level of antiviral activity. The therapeutic index for CB5300 was greater than 177, compared to that of the current prescription interferon alpha for Hepatitis C, which has a therapeutic index of greater than 55.

"There are currently more than 130 million people infected with Hepatitis C worldwide, and the annual cost for treatment of Hepatitis C is greater than \$2 billion in the US alone," Prendergast said.

With the positive pre-clinical results and the opportunity to begin a human clinical trial with the US Department of Defense, Canopus BioPharma is actively seeking a licensing or co-development partner to assist in bringing CB5300 to commercialization.

#### **About Canopus BioPharma, Inc.**

Canopus BioPharma, Inc. (CBIA:CBIA CBIA,) is dedicated to providing the safest, most cost effective and efficacious pharmaceutical products and assay methods in the areas of infectious disease, radiation protection, cancer, and addiction. With innovative science, proven research and development leadership, and superior products and compounds, Canopus BioPharma has, since 2001, been committed to becoming a market trend setter in a new era of healthcare. In addition, the Company is a world leader in the development of novel camelid antibody products to provide unique avenues of progress and improvement in assay methods and monitoring capabilities for physicians, patients and researchers, initially for food chain protection applications. Canopus maintains staff in Australia, South Africa, Ireland, and the USA. Additional information on the company is available at [www.canopusbiopharma.com](http://www.canopusbiopharma.com).

*SOURCE: Canopus BioPharma, Inc.*

### **Metformin Improves Antiviral Response Rates in Chronic Hepatitis C: Presented at AASLD**

<http://www.docguide.com>

By Em Brown SAN FRANCISCO -- November 3, 2008 -- Patients with chronic hepatitis C virus (HCV) infection who have responded poorly to standard antiviral treatment in the past may get a bump in viral response rates if the antidiabetic agent and insulin sensitiser **metformin** is added to pegylated interferon (PEG-IFN) alfa-2a and ribavirin, according to findings presented at the Liver Meeting 2008, the 59th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD). The late-breaking clinical trial results were described here on

November 2 in a special presentation of research highlights, moderated by AASLD President Arthur J. McCullough, MD, Case Western Reserve University, Cleveland, Ohio. The prospective, multicentre, double-blinded, placebo-controlled trial (TRIC-1), led by Manuel Romero-Gomez, MD, Hospital Universitario de Valme, Seville, Spain, involved 125 consecutive patients with chronic HCV genotype 1 infection and insulin resistance, who were randomised to receive either metformin 425 mg 3 times a day during the first month, followed by metformin 850 mg 3 times a day from weeks 4 to 48, or placebo. All subjects were also given standard therapy with PEG-IFN alfa-2a 180 mcg weekly and ribavirin 1,000 to 1,200 mg daily. Baseline characteristics were similar between the study group and controls. The mean age was 47 years (+- 8 years) in the metformin group and 48 years (+- 8 years) in the placebo group. Baseline viral load was 6.33 log<sub>10</sub> IU/mL (+- 0.73 log<sub>10</sub> IU/mL) in the study group and 6.48 log<sub>10</sub> IU/mL (+- 0.76 log<sub>10</sub> IU/mL) in controls.

Virological response was assessed at 4, 12, 24, and 72 weeks in an intention-to-treat analysis.

Dr. Romero-Gomez reported that at week 12, viral clearance had occurred in 54.2% of metformin-treated patients compared with 48.4% of controls. At 24 weeks, 74.6% and 75% of patients showed viral clearance in the 2 groups, respectively. At 72 weeks, the sustained viral response (SVR) rates were 52.5% with metformin and 42.2% without it.

Women (n = 54) showed a stronger response to the addition of metformin than men, with viral clearance at week 12 occurring in 57.7% of women compared with 39.3% of men. At week 24, 80.8% of women and 71.4% had viral clearance and SVR rates at 72 weeks were 57.7% in women and 28.6% of men (P = .031).

"Viral load decreased during the first 12 weeks in a gender-dependent manner," Dr. Romero-Gomez noted. Viral load dropped 4.18 log<sub>10</sub> IU/mL (+- 1.18 log<sub>10</sub> IU/mL) in women and dropped 4.02 log<sub>10</sub> IU/mL (+- 1.68 log<sub>10</sub> IU/mL) in men (P = .044).

Triple therapy was well tolerated, the investigators reported. Adverse effects were largely gastrointestinal, particularly mild diarrhoea, occurring in 34.1% of patients on metformin and 11.4% of patients on PEG-IFN alfa-2a alone (P < .05).

Metformin demonstrated a greater response among women who were heavier than among those who were leaner; however, "these patients were not particularly heavy, overall," explained Dr. McCullough during the special presentation.

"Many patients with chronic HCV infection have insulin resistance," noted Dr. McCullough. "Fat in the liver inhibits response to antiviral therapy. Increasing insulin sensitivity should improve response to treatment."

Results demonstrated that insulin sensitivity increased in patients receiving metformin, but not in those given placebo.

"Women have more fat stores," Dr. McCullough explained. "Metformin improves their response, but at 57.7%, response rates are still low, overall."

Funding for this study was provided by F. Hoffmann-La Roche Ltd.

[Presentation title: Metformin With Peginterferon Alfa-2a and Ribavirin in the Treatment of Naïve Genotype 1 Chronic Hepatitis C Patients With Insulin Resistance (TRIC-1): Final Results of a Randomized and Double-Blinded Trial. Abstract LB6]

## ***AASLD: Mortality Risk in HCV-Positive Transplant Patients Similar Regardless of Donor Status***

<http://www.medpagetoday.com>

By Charles Bankhead, Staff Writer, MedPage Today

Reviewed by Dori F. Zaleznik, MD; Associate Clinical Professor of Medicine, Harvard Medical School, Boston.

SAN FRANCISCO, Nov. 4 -- Hepatitis C-positive liver transplant recipients live just as long whether the donor is HCV-positive or -negative, data from the national transplant network suggest.

HCV-positive organ recipients lived an average of 8.28 years after receiving a liver from an HCV-positive donor, Patrick G. Northrup, M.D., of the University of Virginia in Charlottesville, reported here at the annual meeting of the American Association for the Study of Liver Diseases.

After adjustment for known mortality risks associated with HCV, the survival did not differ from the 10-year mean among HCV-positive patients who received livers from HCV-negative donors.

"It looks like recipients with hepatitis C can receive an organ from someone with the hepatitis C antibodies and do as well as they would with a non-hepatitis C donor," said Dr. Northrup. "That's with careful patient selection."

The need for donor livers far exceeds the supply, and extended-criteria donor selection has offered a partial solution to the organ shortage, Dr. Northrup noted. Use of HCV-positive grafts for HCV-positive patients offers an example of marginal-donor expansion.

Cirrhosis secondary to HCV infection has accounted for as many as half of all liver transplants performed in the U.S., and more than four million people are currently infected, Dr. Northrup continued.

The issue of transplanting organs from HCV-positive donors has particular relevance in that population of liver transplant patients, he said, but the long-term consequences and outcomes had not been carefully studied.

So Dr. Northrup and colleagues analyzed the United Network for Organ Sharing/Organ Procurement and Transplantation Network dataset to identify all adult liver transplantations from January 1994 to February 2008 involving HCV-positive donors.

Patient and graft survival were assessed separately, accounting for donor and recipient HCV status.

Of 70,071 liver transplantations evaluated, 23,972 involved HCV-positive recipients, and 1,313 transplant procedures involved HCV-positive donors.

Three-fourths of HCV-positive donor organs went to HCV-positive recipients, and the remaining organs were given to HCV-negative patients in rare and extreme circumstances, said Dr. Northrup.

Transplants involving HCV-negative donors and recipients were associated with the best survival, an average of 11.7 years.

From that subgroup, mean survival decreased to 10.0 years for HCV-positive patients and HCV-negative donors; 8.28 years for HCV-positive donors and HCV-positive recipients; and 6.33 years for HCV-negative patients who received organs from HCV-positive donors.

HCV-negative patients who received livers from HCV-positive donors had the worst Model for End-Stage Liver Disease (MELD) score and more severe illness.

The researchers developed a survival model that adjusted for multiple variables known to affect survival after transplantation.

Using survival associated with transplants involving HCV-negative patients and donors as the reference, the investigators found that all other combinations increased the mortality hazard ratio by about 20%.

The mortality difference achieved statistical significance for the combination of HCV-positive recipients and HCV-negative donors (HR 1.21, 95% CI 1.17 to 1.25, P<0.0001), and HCV-positive recipients and HCV-positive donors (HR 1.23, 95% CI 1.08 to 1.40, P=0.002).

"After adjusting for known mortality risk factors in an HCV-positive recipient using multivariable proportional hazards survival models, we found that a potential recipient with HCV cirrhosis is not subjected to excess mortality if an HCV-positive liver allograft is used," Dr. Northrup said.

The study was supported by the Jan Albrecht Commitment to Clinical Research in Liver Diseases and the American Association for the Study of Liver Diseases.

The authors reported no conflicts of interest.

**Primary source:** *Hepatology*

**Source reference:**

Northrup PG, et al "Hepatitis C positive liver transplant recipients who receive grafts from donors with hepatitis C antibodies have similar outcomes to hepatitis C negative donors" *Hepatology* 2008; 48(4): 540A. Abstract 524.

Nov 5, 2008

***SciClone Pharmaceuticals' hepatitis C drug candidate thymalfasin fails late-stage study***

<http://money.cnn.com>

NEW YORK (Associated Press) - Biotechnology company SciClone Pharmaceuticals Inc. and partner Sigma-Tau S.p.A. said Wednesday their hepatitis C drug candidate failed to meet its treatment goal in part of a late-stage study.

The companies said **thymalfasin** did not prompt a response in patients who had previously been treated with a combination of pegylated interferon alpha and ribavirin. Those two drugs are often used to treat hepatitis C, a blood-borne virus that affects the liver.

The late-stage, or Phase III clinical trial involved 552 patients either receiving thymalfasin or placebo. All were also given combinations of pegylated interferon alpha and ribavirin.

In a smaller portion of the study involving 182 patients, the company said the drug did meet its goal of treating hepatitis C. That group of patients completed the full 48-week treatment course.

"We are disappointed that the study did not reach its primary efficacy endpoint in the intent to treat population.," said President and Chief Executive, in a statement. "Nevertheless, the data seen in the completer population suggest a potential benefit of using thymalfasin in patients who completed the full course of treatment."

Thymalfasin is already approved in several countries outside the U.S. under the brand name **Zadaxin** for a range of conditions, including hepatitis B and hepatitis C.

## ***AASLD: Hepatologists Eye Protease Inhibitors for Hepatitis C***

<http://www.medpagetoday.com>

By Michael Smith, North American Correspondent, MedPage Today

Reviewed by Robert Jasmer, MD; Associate Clinical Professor of Medicine, University of California, San Francisco

SAN FRANCISCO, Nov. 4 -- Drugs that inhibit the protease enzyme of hepatitis C attracted considerable interest at the American Association for the Study of Liver Diseases meeting here.

Several protease inhibitors are in the pipeline, but the two closest to market are boceprevir and telaprevir. On the basis of phase II data, both were the subject of several presentations here.

So far, both drugs appear to be effective with acceptable side effect profiles, according to Arthur McCullough, M.D., of the Cleveland Clinic, who is president of the liver association and was not involved in the studies.

He added that the new drugs offer the chance to improve on standard therapy for chronic HCV. "If we are only getting a 45% (sustained virological response), we need to do something else," Dr. McCullough said.

One experiment reported with boceprevir almost doubled sustained virological response, which would be "a significant advance" if it holds up in phase III clinical trials, he said.

That investigation involved a four-week lead-in with pegylated interferon and ribavirin -- the standard of care for HCV -- before adding boceprevir for another 44 weeks, said Paul Kwo, M.D., of Indiana University in Indianapolis.

Dr. Kwo, the principal investigator of the so-called SPRINT-1 study, said that after the 48 weeks of treatment, the sustained virological response (measured after 12 weeks of follow-up) was 74%.

In contrast, the sustained virological response in the control arm -- just interferon and ribavirin -- was 38%.

"That's tremendous, that's a delta," he said, using the mathematical term for a change.

The study randomized 595 patients to one of five arms:

- Standard therapy with interferon and ribavirin, whose volunteers acted as controls
- A 28-week arm with all three drugs
- A 28-week arm, starting with a four-week interferon/ribavirin lead-in, followed by all three drugs for 24 weeks
- A 48-week arm with all three drugs
- And a 48-week arm starting with a four-week interferon/ribavirin lead-in, followed by all three drugs for 44 weeks

The last arm has the investigators most excited, but all of the investigational arms outperformed controls, although Dr. Kwo said the researchers will have to wait for further analysis to see if the differences are statistically significant.

It also seems clear, he said, the some patients will do well on the shorter arms and "the challenge" will be to figure who will need the longer therapeutic period.

It is also still not clear which patients will do better with the lead-in, he said.

The two main adverse events that were linked to the drug were dysgeusia -- a bad taste in the mouth -- and about a 0.5 to 1.0 gram per deciliter reduction in hemoglobin levels in addition to the anemia caused by ribavirin.

"That's (the anemia) not concerning, but it's real," he said.

Investigators looking at the other drug, telaprevir, are focusing on shorter therapeutic durations, according to Stefan Zeuzem, M.D., of J.W. Goethe University Hospital in Frankfurt, Germany.

Dr. Zeuzem reported that the final results of the so-called PROVE2 study, conducted in Europe, show that the time for first undetectable level of hepatitis RNA is markedly shortened by the addition of telaprevir to standard medications.

Like the boceprevir trial, the PROVE2 study had several arms:

- A control arm, in which 82 patients got a placebo plus pegylated interferon and ribavirin for 12 weeks, followed by 36 weeks of interferon and ribavirin alone
- An arm in which 78 patients got telaprevir and interferon alone for 12 weeks

- An arm in which 82 patients got telaprevir plus interferon and ribavirin for 12 weeks
- And an arm in which 81 patients got telaprevir plus interferon and ribavirin for 12 weeks, followed by interferon and ribavirin for another 12 weeks

The key efficacy result was that the two arms containing both telaprevir and ribavirin did better at most time points than the control arm, Dr. Zeuzem said.

"The addition of ribavirin leads to better efficacy," he said.

The sustained virological response of the two telaprevir/ribavirin arms was 60% and 69%, respectively, compared with 46% for the control arm, Dr. Zeuzem reported.

The difference was significant (at  $P=0.004$ ) for the 24-week arm, but fell short of significance for the 12-week arm, he said, although improvements in response were significant at earlier times in the study.

The most common adverse events leading to stopping the trial were rash and pruritis, all in the experimental arms, Dr. Zeuzem said. All told, 12 patients, or 7%, discontinued all study drugs due to rash, which was typically maculopapular exanthema.

Late-stage clinical trials for both drugs are under way.

### ***AASLD: Study Clarifies Pediatric HCV Treatment***

<http://www.medpagetoday.com/>

By Michael Smith, North American Correspondent, MedPage Today  
Reviewed by Zalman S. Agus, MD; Emeritus Professor  
University of Pennsylvania School of Medicine.

SAN FRANCISCO, Nov. 5 -- Children with hepatitis C can be treated using the same drugs adults are given, results of the first major randomized trial in young people indicate.

Children ages five to 18 with hepatitis C should be treated with pegylated interferon alpha2a and ribavirin, exactly as adults are, Kathleen Schwarz, M.D., of Johns Hopkins University School of Medicine, told a plenary session at the American Association for the Study of Liver Diseases meeting.

Dr. Schwarz said an estimated 133,000 children in the U.S. have antibodies to hepatitis C and about 66,000 of them are viremic. "They have a definite -- although as yet unquantified -- lifetime risk of cirrhosis and liver cancer," she said.

The current approved therapy for children is un-pegylated interferon plus ribavirin, Dr. Schwarz said, which has a sustained virological response rate of about 46%.

Pegylated interferon monotherapy has been shown to have exactly the same response rate, Dr. Schwarz said, so she and her colleagues conducted the PEDS-C trial to see what would happen if they added ribavirin to the mix.

They enrolled 114 children, with an average age of 10, and randomized them to pegylated interferon at 180 micrograms per 1.73 meters squared once a week, plus ribavirin at 15 milligrams per kilogram of body weight daily or a matching placebo.

The children were treated for 48 weeks and followed for up to 76 weeks, Dr. Schwarz said.

The proportion of children who had a sustained virological response was 53% for those getting the combination and 21% for those on monotherapy, the researchers found, a difference that was significant at  $P=0.001$ .

The same pattern was seen for most subgroups, Dr. Schwarz said, including males, whites, non-whites, and those younger than 11.

Children with the difficult-to-treat genotype-1 had a response rate of 47% if they got the combination and 17% if they got monotherapy, while the comparable figures for other genotypes were 80% and 36%. The differences were significant at  $P=0.003$  and marginally significant at  $P=0.056$ , respectively.

Adverse events did not differ significantly between the two arms of the study, Dr. Schwarz said.

Both groups had anemia and neutropenia that was significant (at  $P<0.05$ ) by week 24 of treatment but was back to baseline at the end of the 72 weeks of follow-up.

The bottom line of the study is that "in children, you can now treat the disease safely" using the same approach used in adults said Arthur McCullough, M.D., of the Cleveland Clinic, who is president of the liver association and was not involved in the study.

The study shows that pegylated interferon and ribavirin have "the exact same kinetics and response as in adults," Dr. McCullough said.

William Balistreri, M.D., of Cincinnati Children's Hospital, concurred, calling the study "seminal and very important -- it will really guide our treatment strategies for children."

He noted that -- as in adults -- children with genotype 1 disease had a response rate that approached 50%, while those with other genotypes did much better.

## **University of Nottingham and Lipoxen plc join forces to fight liver disease**

<http://media-newswire.com>

*Researchers aim to deliver antiviral drugs direct to the liver, by means of nanoparticles and liposomes that will target the affected organ more specifically, to suppress or eliminate the virus, as well as reducing the harmful side effects of untargeted treatment.*

(Media-NewsWire.com) - The University of Nottingham has joined forces with biopharmaceutical company Lipoxen plc to develop improved drug delivery methods for the treatment for viral hepatitis.

Researchers aim to deliver antiviral drugs direct to the liver, by means of nanoparticles and liposomes that will target the affected organ more specifically, to suppress or eliminate the virus, as well as reducing the harmful side effects of untargeted treatment.

Lipoxen plc, a bio-pharmaceutical company specialising in the development of high-value biological therapies including vaccines and oncology drugs, has entered into a research agreement with The University of Nottingham to develop new enhanced formulations of antiviral drugs for the treatment of liver diseases such as viral hepatitis caused by hepatitis C ( HCV ).

The two parties will test novel proprietary formulations based on liposome and nanoparticle delivery in order to achieve enhanced therapeutic effects, by delivering the drugs directly to the liver. This approach is also expected to reduce the toxicity of antiviral drugs used to treat liver disease, by limiting their uptake by surrounding tissues and by red blood cells. The project is receiving funding from the East Midlands' bioKneX Industrial Partnership Scheme.

Hepatitis due to hepatitis C virus infection is a growing problem already affecting 150-200 million people worldwide. In recent years the pharmaceutical industry has invested considerable sums in attempts to develop new drugs for hepatitis C, but unfortunately nearly all of these drugs have failed in clinical development, or have met with only limited commercial success — mainly due to systemic toxicity that has harmful side-effects on other parts of the body besides the liver.

Lipoxen and The University of Nottingham's project is designed to address this systemic toxicity of anti-hepatitis C drugs, which limits the dose at which they can be administered and thereby compromises their efficacy, by engineering their selective delivery to the liver using nanoparticles and liposomes. By improving delivery of the drug specifically to the affected organ, the project seeks to greatly improve the efficacy of anti-hepatitis C drugs by allowing them to be given at higher — ie. more effective — doses.

The two parties will initially work on developing a new proprietary “super generic” formulation of ribavirin, the most commonly used antiviral drug to treat viral hepatitis. This commercially attractive product, which will be based on liposome or nanoparticle delivery, will be used in combination with pegylated–interferon. This combination is the currently accepted optimal regimen for treatment of chronic hepatitis C.

Once this has been achieved the two parties intend to look at improving the delivery of other antiviral drugs for the treatment of hepatitis C that have failed to reach the market due to problems which could potentially be resolved by these novel formulation technologies. Failed anti-hepatitis C drugs include development candidates from, amongst others, GlaxoSmithKline, Boehringer Ingelheim and Wyeth.

Will Irving, Professor of Virology at The University of Nottingham, said: “We are delighted to be involved in this exciting project. If we can succeed in delivering increased doses of ribavirin to the infected liver through our novel delivery systems, it is highly likely we will improve treatment response rates, which are currently limited mostly by the amount of ribavirin an individual patient can tolerate. In addition, such a 'proof of principle' would open up other opportunities for the use of powerful antiviral drugs that are also limited by their systemic toxicities.

“We have a long-term research programme into many aspects of hepatitis C virus infection in The University of Nottingham, and have developed systems in the laboratory for testing drug activity which will underpin our experiments in this project. Lipoxen have an established track record of production of liposomal formulations, so this is an ideal partnership. In addition, we are planning to test and compare polymer nanoparticle delivery vehicles with liposomes, taking advantage of the considerable expertise in nanoparticle technology that exists within The University of Nottingham.”

M. Scott Maguire, Chief Executive Officer of Lipoxen, said: “We are very excited to be working with The University of Nottingham on this project as we believe that by combining our expertise in liposomal and nanoparticle drug formulation with their tissue engineering and molecular virology expertise, we can develop a new “direct to liver” delivery solution to improve the effectiveness of hepatitis C drugs.

“Our initial target will be to demonstrate the value of this new delivery approach using ribavirin, the most widely-used drug globally to treat viral hepatitis.

“Once we have developed this new formulation we believe we can significantly extend its commercial potential in the field of drug delivery to the liver by taking advantage of the opportunity to resurrect several 'near-miss' new drug candidates from major pharma companies that were being developed for the treatment of HCV infection.”

### ***Major Blow for Patients Fearful of Hepatitis C***

<http://www.lasvegasnow.com>

A judge has ruled that a class action lawsuit will not go forward against clinics involved in the hepatitis C outbreak. The ruling affects patients who were not infected with hepatitis C, but still had to go through days and months of anxiety.

Now if they want justice, they'll have to file a lawsuit on their own.

70-year-old Eugenia Hedstrom will never forget the day she found out unsafe injection practices at a clinic may have put her life in danger, "It is frightening. They are telling me that I possibly have AIDS or hepatitis, so it really scared me."

After getting tested, she and thousands of others waited days for her results while anxiety built, "It's very stressful because I also have a son to care for and if something happens to me, what is going to happen to him? So that made it worse. It was bad."

Even though she tested negative, Hedstrom feels she deserves some compensation. Thousands feel the same. But Judge Allan Earl denied to grant class action status for non-infected patients.

Attorney Robert Cottle has more than 4,500 patients who tested negative, "To not have class status granted, it is very difficult. Especially for a lot of my clients who are elderly, 50 or older, because that's the kind of people who went to the clinics for those procedures. So they are very worried they will never see any justice."

Eyewitness News contacted Judge Earl but he declined to comment on his decision.

"Now they have just put a big roadblock in their way and they don't know what they are going to do," said Cottle.

All hope is not lost. Patients have until February of 2009 to file their own lawsuit, but attorneys say a patient's litigation costs might be more expensive than what they could win in a lawsuit, making it risky to even try.

Cottle says a class action lawsuit was supposed to make it economically feasible for everyone. Now it's every patient for themselves.

"I don't think it is fair to all of the people who are involved in this," said Hedstrom.

Judge Earl is expected to release an order explaining why he made the decision to deny class action status.

The option to file with other patients is still there. But because of this decision we could see thousands of lawsuits filed which could take years before they all go to trial.

### ***Anadys starts dosing studies for hepatitis C drug***

<http://www.pharmabiz.com>

Anadys Pharmaceuticals, Inc has initiated dosing **ANA773** in patients chronically infected with hepatitis C virus (HCV) in Part B of a two-part protocol designed to test ANA773 in both healthy volunteers and HCV patients. ANA773 is the company's investigational oral TLR7 agonist prodrug. In Part B of the study, patients in the first cohort will receive 800 mg of ANA773 every other day for 28 days. Doses for subsequent cohorts will be selected based on viral load and tolerability data from the 800 mg cohort.

"The initiation of patient dosing in this study of ANA773 marks the second study that Anadys has initiated in HCV patients this quarter, having commenced patient dosing earlier this week with ANA598, our non-nucleoside polymerase inhibitor," said Steve Worland, president and CEO of Anadys. "With two independent and potentially complementary HCV programmes advancing toward viral load data, we look forward to demonstrating the breadth of our portfolio in this important therapeutic area."

In Part B of the study, patients in the first cohort will receive 800 mg of ANA773 every other day for 28 days. Doses for subsequent cohorts will be selected based on viral load and tolerability data from the 800 mg cohort. Anadys expects to have viral load data from the 800 mg cohort in the first quarter of 2009 and a complete data set in the second quarter of 2009.

In July, Anadys announced that it was resuming clinical investigation of the TLR7 mechanism in HCV by taking ANA773 into a clinical trial under a two-part protocol designed to test ANA773 in both healthy volunteers and patients with HCV. In October, Anadys completed dosing in healthy volunteers. Subjects received a single dose followed by four doses taken every other day, at levels from 200 mg to 1600 mg (with six subjects receiving active and two receiving placebo

in each dose cohort). No serious adverse events were reported. Biomarker induction indicative of immune activation was seen in a majority of subjects beginning at 800 mg. Some side effects commonly seen with interferon treatment, including fever and chills, were observed at higher doses, with the frequency and intensity of interferon-like side effects increasing with dose. One subject at the 1200 mg dose and two subjects at the 1600 mg dose discontinued from the trial before completion of dosing.

ANA773 is an orally administered prodrug of a novel TLR7-specific agonist. Results from preclinical pharmacology studies have shown that ANA773 can elicit desired immune responses and that the profile of response can be modulated by both dose and schedule of administration. Results of completed 13-week GLP toxicology studies have shown that with every-other-day dosing of ANA773, immune stimulation of a magnitude believed to confer therapeutic potential can be achieved without adverse toxicology findings. The immune stimulation observed with every-other-day dosing of ANA773 in monkeys included induction of interferon-alpha and interferon dependent responses at levels that are sustained over 13 weeks of dosing.

Anadys Pharma is a clinical-stage biopharmaceutical company dedicated to improving patient care by developing novel medicines in the areas of hepatitis C and oncology.

Nov 6, 2008

## ***Reversal of Fibrosis and Cirrhosis Seen With Long-Term Entecavir for Chronic HBV***

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

By Martha Kerr

SAN FRANCISCO (Reuters Health) Nov 05 - Long-term treatment with the nucleoside analogue **entecavir (Baraclude**; Bristol-Myers Squibb) in patients with chronic hepatitis B virus (HBV) infection results in reversal of fibrosis and, in some milder cases, cirrhosis, investigators reported here at the annual meeting of the American Association of Liver Diseases.

Entecavir, approved in 2005 for the treatment of chronic HBV infection in adults, has selective anti-HBV activity. Results of a study with a median follow-up of 6 years, presented by Dr. Yun-Fan Liaw of Chang Gung Memorial Hospital in Taipei, Taiwan, showed that the drug not only reduces viral load but also improves liver histology.

The study involved 63 patients with chronic HBV infection, 47 of whom were HBeAg-positive. At baseline, the mean HBV DNA level was 9.2 log<sub>10</sub> copies/mL, the mean Knodell necroinflammatory score was 7.9, and the mean Ishak fibrosis score was 2.4.

Biopsies were available from 57 patients after a median entecavir treatment time of 6 years.

Among the four patients with baseline cirrhosis (an Ishak fibrosis score of 5 or greater), there was an improvement in Ishak fibrosis score of 1 or greater, with a median change from baseline of -3.

"These data suggest that long-term treatment with entecavir has the potential to stop liver damage and may even improve liver fibrosis caused by chronic hepatitis B infection," Dr. Liaw told meeting attendees.

"The ability to provide effective long-term treatment with a potent antiviral with minimal resistance represents a positive step forward."

Japanese researchers reported similar findings in a study of 66 nucleoside-naive patients and 84 lamivudine-refractory patients with chronic HBV genotype C infection who were treated with entecavir for more than 96 weeks.

Dr. Y. Katano and colleagues at Nagoya University in Aichi reported that "there were significant improvements from baseline in Knodell necroinflammation and fibrosis for both nave and lamivudine-refractory patients" after a mean of 148 weeks of entecavir treatment.

"Notably, treatment beyond 48 weeks resulted in continued improvement in fibrosis scores in both nave and lamivudine-refractory patients." Dr. Katano said.

## ***AASLD 2008: High Coffee Consumption May Slow Hepatitis C Progression***

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

Laurie Barclay, MD

November 6, 2008 (San Francisco, California) — Increased coffee consumption may slow the progression of liver damage caused by hepatitis C virus infection, researchers reported in a poster here at The Liver Meeting 2008: 59th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD). Patients who self-reported drinking 3 or more cups of coffee per day were less likely to have liver disease progression than those who drank less coffee daily.

"In population studies, coffee intake has been inversely associated with cirrhosis, chronic liver disease, and hepatocellular carcinoma. But, no studies have examined the relationship between coffee consumption and progression of advanced liver disease," wrote Neal D. Freedman, MD, of the National Cancer Institute at the National Institutes of Health, Department of Health and Human Services, in Rockville, Maryland, and colleagues.

To study this relationship, Freedman analyzed patient questionnaire data about food frequency, including coffee and tea consumption, from the 3.5-year HALT-C randomized trial of 1050 hepatitis C patients at Ishak stage 3 or higher who were unresponsive to standard drug therapies. Some patients in the HALT-C trial received no treatment, and others received 90 µg/week of pegylated interferon alfa-2a.

Of the 808 patients who responded to the questionnaire at baseline, 711 drank zero to 2 cups of coffee a day, and 97 drank 3 or more cups of coffee daily. Those who drank the most coffee also consumed the most alcohol and cigarettes. These coffee drinkers, however, had healthier livers than the other participants, with less steatosis (evaluated by biopsy) and lower bilirubin levels,  $\alpha$ -fetoprotein levels, and aspartate aminotransferase/alanine aminotransferase ratios ( $P < .05$ ).

Liver disease had progressed in 208 patients at the 13-month follow-up, but outcome rates decreased from 10.4/100 person-years (no coffee daily) to 6.0/100 person-years (3 or more cups of coffee daily;  $P = 0.002$ ). The hazard ratio for coffee consumption ranged from 1.21 (0.81 - 1.79) for no coffee daily to 0.53 (0.29 - 0.95) for 3 or more cups daily (95% confidence intervals;  $P = .0005$ ). The results show that "coffee consumption may slow the progression of fibrotic liver disease," Freedman wrote in the abstract.

"This is an observational study," Freedman told *Medscape Gastroenterology*, "so it may be that coffee is a marker for some other activity," he said. "It may be that people who are feeling sicker don't drink as much coffee." He looked at tea drinkers as well but did not find an association between tea consumption and liver disease, he said.

The questionnaire did not ask about the strength of the coffee, what people put in their coffee, or whether people drank caffeinated or decaffeinated coffee, Freedman said. About 85% of coffee consumed nationally is caffeinated. Freedman said that hypotheses about what part of coffee is beneficial to the liver are "pretty speculative" although "maybe the best data is for caffeine." Of the 1000-plus compounds in coffee, several of them may be influencing liver disease, he said.

One advantage of the study was its focus on "the natural history of clinically significant disease progression, which other studies have not been able to do," said Freedman's colleague James Everhart, MD, of the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Department of Health and Human Services, in Bethesda, Maryland. The study also benefited from a homogenous population. "They all started off with liver disease, so we knew they had liver disease and were able to then look at progression of liver disease from that point on," he told *Medscape Gastroenterology*.

Actual coffee consumption can be difficult to measure. Samir Rouabhia, MD, from the Butler University Hospital Center's Internal Medicine Department in Algeria, said that people tend to drink coffee unevenly. "One day you take one cup and one day you take three cups," he told *Medscape Gastroenterology*, which makes it difficult to measure coffee's effect on the liver. He also pointed out that it's unclear how the coffee was prepared and how strong it was.

- Although patients with hepatitis C virus infection who drank the most coffee (3 or more cups daily) also consumed the most alcohol and cigarettes, they had slower progression of fibrotic liver disease. Hazard ratio for progression of liver disease was 1.21 for no coffee daily to 0.53 for 3 or more cups daily (95% confidence intervals;  $P = .0005$ ).
- Those who consumed 3 or more cups of coffee daily had less evidence of liver damage than did other participants with hepatitis C virus infection, with less steatosis on biopsy, and significantly lower bilirubin levels,  $\alpha$ -fetoprotein levels, and aspartate aminotransferase/alanine aminotransferase ratios.

*The Liver Meeting 2008: 59th Annual Meeting of the American Association for the Study of Liver Diseases: Abstract 1778. Presented November 4, 2008.*

## **Triple Therapies Offer Promising Results for Hepatitis C**

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

Laurie Bouck

November 6, 2008 (San Francisco, California) — Two protease inhibitors improve the sustained virologic response (SVR) rate in hepatitis C patients when combined with the standard drug treatment, researchers for 2 separate studies said here at The Liver Meeting 2008, the 59th Annual Meeting of the American Association for the Study of Liver Diseases.

The first study analyzed the use of boceprevir to augment the combination of once-weekly peginterferon alfa-2b (1.5 µg/kg) plus daily ribavirin (400 to 1400 mg).

Data were obtained from 595 patients who participated in the HCV SPRINT-1 phase 2 study of boceprevir 800 mg 3 times a day. That study had 3 treatment groups and 1 control group.

One group received boceprevir after a 4-week lead-in of peginterferon alfa-2b plus daily ribavirin (800 to 1400 mg), then continued receiving all 3 medications for 24 weeks (n = 103) or 44 weeks (n = 103), for a total of 28 or 48 weeks, respectively. The other 2 treatment groups received all 3 medications for the duration of the study; daily ribavirin dose was either 800 to 1400 mg for 28 weeks (n = 107), or 800 to 1400 mg or 400 to 1000 mg for 48 weeks (n = 103). The control group received combination therapy without boceprevir but with daily ribavirin (800 to 1400 mg) for 48 weeks (n = 104).

The 48-week boceprevir lead-in group had the highest SVR rate; 74% of patients were hepatitis C virus (HCV) negative, compared with 38% in the boceprevir-free control group. Viral breakthrough with the triple therapy was more common without the boceprevir lead-in times.

The 4-week lead-in allows "the pegylated interferon and the ribavirin to get to steady-state levels," lead investigator Paul Kwo, MD, from Indiana University School of Medicine in Indianapolis, told Medscape Gastroenterology. Once you have partially reduced the virus, "you add boceprevir to further reduce it," he said. This lead-in strategy also seems to reduce viral resistance through mutations, he said.

The boceprevir groups did have a higher rate of adverse-event-related discontinuations — up to 19%, compared with 8% in the control group. These discontinuations were caused by adverse events related to peginterferon or ribavirin, which boceprevir might have aggravated, said Dr. Kwo. "I think this becomes a matter of being in the clinic and learning to manage the side effects of boceprevir in addition to [peginterferon] and ribavirin."

"I think that's going to be true for all the proteases," Dr. Kwo pointed out. "The second time around, you have more experience with them, and you should be able to have a better adherence rate to the medicine."

The second study, presented by Stefan Zeuzem, MD, from the Department of Internal Medicine at J.W. Goethe University Hospital in Frankfurt, Germany, analyzed the use of telaprevir plus once-weekly peginterferon alfa-2a (180 µg), with or without daily ribavirin (1000 or 1200 mg). Telaprevir was found to be effective in triple therapy for patients with HCV genotype 1.

The PROVE2 study, a 29-site European study, randomized 323 patients to receive various combinations of peginterferon, ribavirin, and telaprevir. The groups were as follows:

- 82 patients received peginterferon alfa-2a plus daily ribavirin (1000 or 1200 mg), plus a placebo for 48 weeks (PR48 group)

- 78 patients received peginterferon alfa-2a plus telaprevir 750 mg every 8 hours for 12 weeks (T12/P12 group)
- 82 patients received peginterferon alfa-2a plus ribavirin plus telaprevir 750 mg every 8 hours for 12 weeks (T12/PR12 group)
- 81 patients received peginterferon alfa-2a plus ribavirin plus telaprevir 750 mg every 8 hours for 12 weeks, followed by 12 weeks of just peginterferon alfa-2a and ribavirin (T12/PR24 group).

In the placebo (PR48) group, 48% achieved SVR at follow-up. In contrast, 68% of the 24-week triple-therapy (T12/PR24) group achieved SVR.

"I think the data look pretty good," session moderator T. Jake Liang, MD, from the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health in Bethesda, Maryland, told Medscape Gastroenterology. The SVR change is "an important improvement in the treatment response," he said. "We will have to see what the registration phase 3 trial shows," he said, but the phase 2 trial is probably "pretty indicative of what the larger trial could be."

Dr. Liang also thought that boceprevir was "another drug that potentially could be an important addition to the treatment mode for hepatitis C," although, he said, "I think we're going to have to wait for the registration trials and see what the outcome is." "Both of these drugs are the leading drugs at this point that we know appear to have increased efficacy over the standard therapy," he said.

Dr. Liang said it was hard to compare the 2 drugs and their studies directly, because the data from different studies are not always comparable.

Dr. Kwo is a member of advisory committees or review panels for Schering-Plough and Vertex; has received grant or research support from Indenex, Human Genome Sciences, Merck, Novartis, Schering-Plough, and Vertex; and has received speaking and teaching support from Novartis and Schering-Plough. Dr. Zeuzem has consulted for Tibotec, Vertex, and Roche; and has investigated off-label uses of telaprevir. Dr. Liang has disclosed no relevant financial relationships.

*The Liver Meeting 2008: 59th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD): Abstracts LB16 and 243. Presented November 3 and 4, 2008.*

## **Hepatitis C transmission not reduced by C-sections**

<http://www.innovations-report.de>

Planned cesarean sections do not help to reduce the chances of a pregnant mother with Hepatitis C (HCV) transmitting the infection to her unborn baby, according to new scientific findings by the National Maternity Hospital in Dublin and University College Dublin.

Hepatitis C is the most common cause of chronic viral infection in the Western World today. It affects an estimated 170 million people worldwide. It is a viral infection of the liver which is mainly transmitted through contact with contaminated blood or blood products.

Infant infection rates are also linked to the number of mothers infected with the viral infection and the risk factors associated with the transmission of the infection to their unborn children in the womb.

The results of a new 5-year study of 559 mother-child pairs in Ireland, one of the largest such studies of its kind, published in the *American Journal of Obstetrics & Gynaecology*, show that vaginal delivery and planned cesarean among mothers infected with Hepatitis C display almost equal transmission rates of Hepatitis C from mother to child (4.2% and 3% respectively).

“The mode of delivery itself was not shown to have a significant influence on the transmission rate of hepatitis C from mother to child,” says Professor Fionnuala McAuliffe from the National Maternity Hospital in Dublin and the School of Medicine and Medical Science at University College Dublin, one of the authors of the report.

“The main risk factor associated with the vertical transmission of hepatitis C was the presence of detectable hepatitis C virus in the mother’s bloodstream, a condition where viruses enter the bloodstream and hence have access to the rest of the body.”

“Mothers who demonstrated detectable hepatitis C virus had a significantly higher transmission rate (7.1%) to their infants compared to the transmission rate (0%) for those in whom the hepatitis C virus was undetectable during pregnancy,” explains Professor McAuliffe.

“According to these new findings, if the Hepatitis C virus is undetectable antenatally despite the mother being antibody positive the patient can be reassured that the risk of vertical transmission to their child is minimal, and this is a significant development for patient counseling.”

## ***Hepatitis C Virus Infection May Be a Risk Factor for Renal Cancer***

<http://www.cancerpage.com>

By Martha Kerr

SAN FRANCISCO NOV 05, 2008 (Reuters Health) - Researchers from Henry Ford Hospital, Detroit, announced here this week that chronic hepatitis C virus infection appears to be a risk factor for primary renal cell carcinoma (RCC).

"We undertook our study when we began to notice what seemed like an unusually large number of patients with kidney cancer coming in to our (hepatology) clinic," principal investigator Dr. Stuart C. Gordon told Reuters Health.

This prompted Dr. Gordon and colleagues to examine Henry Ford Hospital's database to determine the incidence of RCC among HCV-infected patients aged 18 years and older who tested positive for HCV between 1997 and 2008. They were compared with patients who were anti-HCV negative.

The cohort consisted of 74,570 patients, of whom 9,401 were HCV-positive (12.6%).

There were 163 RCC patients among the HCV-negative group and 35 RCC cases among HCV-positive patients. This translates to prevalence rates of 0.25 RCC cases per 100 HCV-negative

patients and 0.37 cases per 100 HCV-positive patients, Dr. Gordon reported at The Liver Meeting 2008, the annual meeting of the American Association for the Study of Liver Diseases.

"The mean age at RCC diagnosis was much younger in HCV+ individuals (52 vs. 63)," the research team found.

The unadjusted odds ratio for RCC with versus without HCV was 1.49. Men between 18 and 50 years of age at HCV diagnosis had an adjusted odds ratio for RCC of 4.8.

While the findings indicate an association between chronic HCV and renal cell carcinoma, especially in young males, the investigators note that the results may have been affected by referral bias at a tertiary medical center, as well as unmeasured risk factors.

**Nov 7, 2008**

## ***HCV Relapse Rates May Be Lower With Peginterferon Alfa-2b Than Alfa-2a***

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

By Martha Kerr

SAN FRANCISCO (Reuters Health) Nov 06 - Results of the IDEAL study reported here this week show that virologic response is equally strong with peginterferon alfa-2a or peginterferon alfa-2b in the treatment of hepatitis C virus (HCV) infection, but viral load reductions are more rapid with peginterferon alfa-2b.

"The faster you can suppress viral levels, the lower the chances of disease relapse," co-investigator Dr. Paul Kwo of Indiana University in Indianapolis told Reuters Health.

IDEAL compared combination therapy with one of two doses of peginterferon alfa-2b (Peg 2b) and ribavirin with peginterferon alfa-2a (Peg 2a) and ribavirin in 3,070 patients with HCV genotype 1 infection.

The results showed that virologic response was similar for all three treatment regimens at 12 weeks, Dr. Mark S. Sulkowski of Temple University School of Medicine in Philadelphia, Pennsylvania, reported at the annual meeting of the Association of the study of Liver Diseases.

Also, the magnitude of change in HCV RNA at treatment week 4 was highly associated with the likelihood of sustained virologic response. Peg 2b achieved a greater HCV RNA reduction at 4 weeks.

"Patients with a decline in HCV RNA from baseline of greater than 3 log<sub>10</sub> (at week 4) had a greater than 61% probability of sustained virologic response, while those with a decline of less than 1 log<sub>10</sub> had a less than 5% probability of sustained virologic response," Dr. Kwo reported.

"Treatment weeks 4 and 12 remain the mainstay for physicians to make decisions regarding the ability of patients to achieve sustained virologic response," the IDEAL researchers say.

## ***First results from MURDOCK Study revealed at San Francisco conference***

<http://www.salisburypost.com>

By Emily Ford

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KANNAPOLIS — The first research results to emerge from the MURDOCK Study were presented last week at an international conference in San Francisco, giving hope to people who suffer from hepatitis C.

Duke University scientists and physicians working for the study, which is named for N.C. Research Campus founder David Murdock, have discovered an important genetic clue that may help unlock the mystery of hepatitis C infection.

"I'm incredibly excited about it," said Dr. John McHutchison, a lead investigator for the MURDOCK Study and associate director of the Duke Clinical Research Institute.

McHutchison's team has identified a set of proteins that may be able to predict who will most likely respond to standard therapy for hepatitis C infection.

Only about 50 percent of patients who undergo the grueling regimen are cured, but doctors have not been able to predict which patients will benefit and which will just suffer side effects.

This development could prevent patients from undergoing the regimen if they probably would not respond anyway.

Without support from the MURDOCK Study, "I would not have thought I would have the ability to do such a thing," McHutchison said. "I have tried for 10 years without success."

The research was presented at the annual meeting of the American Association for the Study of Liver Disease. More than 7,000 researchers from 55 countries attended.

Murdock, owner of Dole Food Co., gave Duke \$35 million last year to launch the study, which will try to better understand hepatitis C, heart disease, obesity and arthritis using genomic technologies.

Now that the Core Laboratory at the Research Campus has opened, the MURDOCK Study will move much of its work to Kannapolis. The initial research into hepatitis C was conducted using blood and tissue samples that have been stored for years at Duke.

Murdock provided the money to hire people to conduct the initial research.

The study wants to enroll 50,000 volunteers from Kannapolis and Cabarrus County for future research phases.

McHutchison cautioned that the results announced in San Francisco are just a first step. His team hopes to conduct a clinical trial in about a year.

Dr. Keyur Patel presented the findings. Additional Duke scientists on the team include Laura Dubois, Will Thompson, Joe Lucas, Art Moseley Diane Uzarski, Hans Tillman, Robert Califf and Jeanette McCarthy.