

HCV ADVOCATE WEEKLY NEWS REVIEW

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

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Week Ending: June 18th, 2005

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June 13th, 2005

County Considers Needle-Exchange Program

SourceURL:<http://www.koin.com/>

Programs Aim At Combating Hepatitis C, HIV

BEND, Ore. -- Deschutes County health officials are considering a needle-exchange program for intravenous drug users as a way to reduce rates of hepatitis C and HIV infection in Central Oregon.

Drug users would be given clean equipment from Deschutes County Health Department employees in order to limit the spread of disease.

Seven counties in Oregon, including rural Benton County, already have needle-exchange programs to combat rising rates of hepatitis C and HIV.

The increase is blamed partly on increase methamphetamine abuse. Meth addicts frequently inject the drug, carrying the risk of infection when they share needles.

But the needle-exchange proposal worries some elected and law enforcement officials, including Deschutes County Sheriff Les Stiles.

He says health officials have to try news ways to reduce the number of HIV and hepatitis cases -- but a needle-exchange program carries the unintentional message that it's OK to do drugs.

Novelos Therapeutics Announces Merger With U.S. Public Company - Trading to Begin on Tuesday Under Symbol "NVLT"

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

Merger Coincides With Private Placement of \$2.2 Million

NEWTON, MA--(MARKET WIRE)--Jun 13, 2005 -- Novelos Therapeutics, Inc., a biotech company focusing on oxidized glutathione for use in fighting cancer and hepatitis, today announced it has completed a merger with Common Horizons, Inc., a public company that had no meaningful operations prior to the merger. Novelos Therapeutics, Inc., the surviving entity, is scheduled to begin trading tomorrow, Tuesday, June 14th, under the symbol (OTC BB: NVLT).

Concurrently with the merger, the Company completed the first round of a private offering of Units to accredited investors. The Company sold 87 Units, each Unit consisting of 20,000 shares of common stock and a three-year warrant to purchase 10,000 shares of common stock at an exercise price of \$2.25 per share, at a purchase price of \$25,000 per Unit. In exchange for the Units sold, the Company received cash proceeds of \$1,725,000, and three investors converted the \$450,000 principal amount outstanding of promissory notes issued by Novelos Therapeutics, for a total of \$2,175,000. vFinance Investments, Inc. and Mercer Capital, Ltd. are the placement agents for the offering.

"This transaction marks an important first step for Novelos Therapeutics to begin to access public capital to implement the development and commercialization plans for our pharmaceutical products addressing cancer and hepatitis. With a publicly traded currency in the form of Novelos common shares, the Company will also be able to consider acquiring additional products or technologies," said Harry Palmin, President and Acting CEO of Novelos Therapeutics.

Mr. Palmin added, "We have a very compelling story: Cancer and hepatitis are huge markets with great unmet needs. Our drugs have been used safely and effectively in thousands of patients in the Russian Federation, where they are patented, produced and sold by an unrelated entity. The Company's world-wide patent position (outside of the former Soviet Union) is solid, and manufacturing is simple, inexpensive and scalable. We have also completed a U.S. Phase I/II non-small cell lung cancer study."

About Novelos Therapeutics, Inc.

Novelos Therapeutics, Inc. was established in 1996 to commercialize two promising oxidized glutathione based compounds, NOV-002 and NOV-205, for the treatment of cancer and hepatitis. Both compounds have completed clinical trials in humans and have been approved for use in the Russian Federation where they were developed. NOV-002, marketed in Russia under the trade name GLUTOXIM®, has been administered to over 5,000 patients, yielding excellent safety and promising efficacy data. A U.S. Phase I/II clinical trial of NOV-002 for lung cancer has been completed. U.S. clinical trials with NOV-205 for hepatitis C are anticipated to commence shortly.

About the Products

NOV-002, the lead compound, is being developed to treat non-small cell lung cancer ("NSCLC"). NOV-002 is a cytoprotectant and an immunomodulator. When used in combination with chemotherapy, NOV-002 increased the one-year survival rate from 17% to 63% in a Russian study, a result that also represents an 80% improvement above the U.S. 35% standard of care. A U.S. Phase I/II clinical study has been completed.

NOV-002 is also being developed to treat refractory (that is, not responsive to chemotherapy) ovarian cancer. Two additional opportunities for NOV-002 are under development, including radiation protection and psoriasis.

NOV-205 is being developed to treat chronic hepatitis C in the U.S. When used as mono-therapy for one month in hepatitis B and for two months in hepatitis C, NOV-205 has been shown to greatly reduce or eliminate viral loads and to vastly improve liver function relative to existing drugs on the market.

This news release contains forward-looking statements. Such statements are valid only as of today, and we disclaim any obligation to update this information. These statements are subject to known and unknown risks and uncertainties that may cause actual future experience and results to differ materially from the statements made. These statements are based on our current beliefs and expectations as to such future outcomes. Drug discovery and development involve a high degree of risk. Factors that might cause such a material difference include, among others, uncertainties related to the ability to attract and retain partners for our technologies, the identification of lead compounds, the successful preclinical development thereof, the completion of clinical trials, the FDA review process and other government regulation, our pharmaceutical collaborators' ability to successfully develop and commercialize drug candidates, competition from other pharmaceutical companies, product pricing and third-party reimbursement.

Consulting For Strategic Growth I, Ltd. ("CFSG") has a June 1, 2005, contract to provide Novelos with consulting, business advisory, investor relations, public relations and corporate development services for a three-month period. In connection with these services, CFSG prepares press releases, corporate profiles, and other publications on behalf of the Company. Independent of CFSG's receipt of cash compensation from the Company, CFSG may choose to purchase the common stock of the Company and thereafter liquidate those securities at any time it deems appropriate to do so.

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Source: Novelos Therapeutics, Inc.

June 14th, 2005

Hep C Outbreak at a Haematology and Oncology Outpatient Clinic

SourceURL: <http://www.gastrohep.com/>

A large health care-associated Hepatitis C outbreak was related to shared saline bags contaminated through syringe reuse, reports the latest *Annals of Internal Medicine*, highlighting the need for effective infection-control programs.

Approximately 3 million persons in the United States have chronic Hepatitis C virus infection.

Health care-associated Hepatitis C transmission can occur if aseptic technique is not followed.

Dr de Oliveira and colleagues suspected a health care-associated Hepatitis C outbreak after 4 infections among patients at the same clinic.

The investigators determined the extent and mechanism of Hepatitis C transmission among clinic patients by an epidemiologic analysis through a cohort study.

The investigative team included patients who visited the haematology/oncology clinic in Nebraska from 2000 through 2001.

Contaminated probably occurred when syringes for drawing blood were reused to withdraw saline solution from shared bags – Annals of Internal Medicine

The team measured Hepatitis C infection status, relevant medical history, and clinic-associated exposures.

The investigators used bivariate analysis and logistic regression to identify risk factors for Hepatitis C infection.

Of 613 clinic patients contacted, the team reported that 494 underwent Hepatitis C testing.

The investigators documented infection in 99 patients who lacked previous evidence of Hepatitis C infection; all had begun treatment at the clinic before 2001.

The team identified Hepatitis C virus genotype 3a in all 95 genotyped samples.

The infection presumably originated from a patient with chronic Hepatitis C who began treatment in 2000.

The investigators found that infection with Hepatitis C was statistically significantly associated with receipt of saline flushes.

The team suggested that shared saline bags were probably contaminated when syringes used to draw blood from venous catheters were reused to withdraw saline solution.

The clinic corrected the procedure of saline flushes in July 2001.

The investigators noted that the delay of more than a year between outbreak and investigation may have contributed to an underestimate of cases.

Dr de Oliveira's team concludes, "This large health care-associated Hepatitis C outbreak was related to shared saline bags contaminated through syringe reuse."

"Effective infection-control programs are needed to ensure high standards of care in outpatient care facilities, such as hematology/oncology clinics."

Ann Int Med 2005; 142(11): 898-902

Innogenetics Sees Three-Year Delay in Hepatitis C Vaccine Launch - Press Report

SourceURL: <http://www.forbes.com>

BRUSSELS (AFX) - Chairman of biotechnology company Innogenetics NV Rudy Marien said that the launch of a vaccine for hepatitis C will be delayed by at least three years due to an extension of clinical trials, according to a report in daily De Standaard.

'It will take at least an extra three years,' he said.

Innogenetics said earlier that the trials were 'inconclusive' and have to be extended by 15 months.

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June 15th, 2005

Hep C: Hope on the Distant Horizon

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

LONDON, June 15 2005- Driven by a favorable epidemiology and high unmet medical need, the hepatitis C pipeline is both rich and varied, consisting of at least 28 drugs belonging to four major classes. Unfortunately, current therapy meets less than 50% of the CHC medical need. However, a new report from independent market analyst Datamonitor* (DTM.L) indicates that while progress in the market is expected to be slow until 2011, the launch of hepatitis C virus (HCV) polymerase and protease inhibitors thereafter is expected to fuel rapid growth. This growth is expected to result in a market value in excess of \$4 billion by 2012 and moreover, a new treatment paradigm may also be established.

Current therapy fails in over half of all chronic hepatitis C patients

The chronic hepatitis C (CHC) treatment market is currently dominated by market leaders Roche and Schering-Plough, who market both components of the CHC standard of care—a combination of pegylated interferon (Peg-IFN) alfa and ribavirin (RBV). Historical growth in the hepatitis C market has been high, with a compound annual growth rate (CAGR) of 28.5% experienced between 1999 and 2003. This was mainly fuelled by the launch of RBV in 1998 and the second-generation interferons, Peg-IFN alfa-2b and -2a in 2000 and 2002, respectively- both of which significantly improved the efficacy of therapy. However, treatment outcomes following Peg-IFN plus RBV combination therapy are highly heterogeneous and depend on the viral genotype with which a patient is infected. Indeed, sustained viral response (SVR) rates in the ‘easy-to-treat’ genotypes 2 and 3 can be up to 88% of cases, says Datamonitor infectious diseases analyst Dr Brigitte de Lima. “In contrast, less than half of those who harbor HCV genotype 1 successfully respond to therapy. Significantly, genotype 1 accounts for between 70-75% of the patient pool in the West and, therefore, current therapy meets less than 50% of the CHC medical need.”

“This has led to the accumulation of patients that have failed first-line therapy with the current standard of care, known as non-responders, and patients who responded to therapy but subsequently relapsed. Moreover, as a result of the slow rate of HCV disease progression, the wave of patients seeking treatment is still gaining momentum and expected to peak from 2014 onwards,” she says.

Incremental improvements in short term likely followed by revolutionary treatment options in long-term.

The combination of high patient potential and significant medical unmet need have attracted big Pharma and small biotech alike, creating a pipeline consisting of 28 drugs in clinical development and a range of potential drug candidates at the preclinical stage. However only 14% of these molecules are currently in Phase III, with none of these specifically targeting the HCV particle per se, Dr de Lima says. “Instead, they act by enhancing the host antiviral response and therefore, no major paradigm changes are expected to occur in HCV therapy for at least the next five years.”

Datamonitor research found that among the three drugs that are closest to market, only Valeant’s RBV follow-up drug viramidine is perceived as a key addition to HCV therapy. The drug has similar efficacy to its predecessor but differentiates itself based on its more favorable toxicity profile.

The highest hopes for effective future HCV therapy are being pegged on the small molecules able to specifically interfere with HCV replication, in particular the NS3 protease inhibitors. This new paradigm was first highlighted as a realistic goal by Boehringer Ingelheim (BI), whose protease inhibitor BILN 2061 demonstrated an unprecedented drop in viral load after only two days of therapy, Dr de Lima says. “However, the enthusiasm was largely dampened when BI was forced to suspend further development of the drug due to cardiac toxicity in animals.”

The mixed emotions left behind among the treating community are best reflected by the following opinion leader comment:

“I think [the most promising class] is your protease inhibitors, if you’re able to get over the problem of toxicity. The results of the Boehringer drug, as regards power, were amazing compared with what we had.” -UK opinion leader

With the most developed protease inhibitor—Vertex/Mitsubishi’s VX-950—still at least seven years from reaching the market, hopes are now centered on the polymerase inhibitors, most notably Idenix/Novartis’s NS5B polymerase inhibitor valopicitabine (NM283). However clinical development has also led to general disappointment when early-stage trials showed only moderate reductions in viral load with NM283 monotherapy. This led to subsequent clinical trials being designed for combination therapy with Peg-IFN, with the end goal of potentially replacing RBV with NM283.

Is future therapy without an interferon backbone realistic?

Early results from the NM283 clinical trials raise the question about the future role of Peg-IFN in HCV therapy: will it remain the backbone for several years to come or eventually fade from use? Datamonitor’s research found that some believe that future HCV therapy is more likely to consist of combination therapy, based on Peg-IFN plus one or more specific antivirals. Others take a more optimistic view nurtured by faith in that antivirals could be capable of curing HCV infection on their own. This dichotomy is reflected by the following two opinion leader comments:

“I see [future HCV therapy] as a multidrug therapy—combination and tailoring the best combination to the individual patient.” -French opinion leader.

“We have to wait and see...Just because every other viral disease is using multidrug therapy, it doesn’t mean you have to.” -UK opinion leader

Given the consequences of untreated HCV infection, which include liver cirrhosis, hepatocellular carcinoma, liver transplant and death, many physicians will require convincing data before replacing a proven therapeutic option with antiviral monotherapy, de Lima says. “As such, Datamonitor expects Peg-IFN to retain a relatively strong market presence, despite the plethora of drugs in the pipeline, resulting in a CAGR of 9.9% for the interferon class between 2004 and 2013.”

Digestive Endoscopy Not a Risk for Hep C Transmission

SourceURL: <http://www.gastrohep.com>

Findings from a study in the most recent *Annals of Internal Medicine* show that properly performed digestive endoscopy is not a major risk factor for the transmission of Hepatitis C.

The potential role of digestive endoscopy as a mode for transmission of Hepatitis C virus is controversial.

Dr Ciancio evaluated the role of digestive endoscopy in transmitting Hepatitis C.

The research team compared the incidence of Hepatitis C infection in a cohort of patients undergoing endoscopy and in a cohort of blood donors.

8260 undergoing endoscopy remained anti-Hepatitis C-negative 6 months after the procedure – Annals of Internal Medicine

The team conducted a prospective cohort study in 3 endoscopic units and 2 blood banks in northwestern Italy.

The potentially exposed cohort consisted of 9188 outpatients consecutively recruited from 3 endoscopic units.

Of 9008 patients negative for antibody to Hepatitis C (anti-Hepatitis C), the team retested 8260 for anti-Hepatitis C 6 months after endoscopy.

The unexposed cohort consisted of 51,230 healthy, anti-Hepatitis C-negative persons who donated blood at 2 blood banks in the same area and during the same time.

The researchers reported that 38,280 of these patients were tested again for anti-Hepatitis C 6 to 48 months after the first blood donation.

The team evaluated differences in the anti-Hepatitis C seroconversion rate between the exposed cohort (patients undergoing endoscopy) and the unexposed cohort (blood donors).

The researchers evaluated seroconversion by a third-generation enzyme immunoassay for anti-Hepatitis C.

Persons positive for anti-Hepatitis C were tested for Hepatitis C RNA by polymerase chain reaction.

The researchers found that all 8260 persons undergoing endoscopy remained negative for anti-Hepatitis C 6 months after the procedure.

None of the 912 patients who underwent endoscopy with the same instrument previously used on Hepatitis C carriers showed anti-Hepatitis C seroconversion.

The research team observed that 4 blood donors became positive for anti-Hepatitis C and Hepatitis C RNA.

The researchers noted that each had undergone minor surgery before the second test.

The team reported that in the endoscopy cohort, 8% of patients were lost to follow-up.

Dr Ciancio's team concludes, "These findings support the hypothesis that properly performed digestive endoscopy is not a major risk factor for the transmission of Hepatitis C."

Ann Int Med 2005: 142(11): 903-9

June 16th, 2005

Causes of Portal Venous Thrombosis in Cirrhotic Patients

SourceURL:<http://www.gastrohep.com>

Prothrombotic mutations by themselves do not cause portal vein thrombosis in cirrhosis, whilst sclerotherapy and previous abdominal surgery favour the development of portal vein thrombosis, finds this month's *European Journal of Gastroenterology & Hepatology*.

Dr Mangia and colleagues compared frequencies of 3 common prothrombotic mutations.

Thrombotic factors considered by the team were factor V Leiden, the G20210A mutation of the prothrombin gene, and homozygosity for C677T methylenetetrahydrofolate reductase.

The researchers included 219 cirrhotic patients, 43 with and 176 without portal vein thrombosis.

Combination of the 2 acquired factors increases the risk for portal vein thrombosis – European Journal of Gastroenterology and Hepatology

Variables related to portal vein thrombosis included prothrombin levels, platelet count, Child-Pugh classification, and previous abdominal surgery.

The researchers also assessed the number of decompensation events, size of varices, red markers on varices, and sclerotherapy.

The research team followed up all patients for a mean period of 18 months.

The team detected prothrombotic mutations in 30% of the cirrhotic patients, at equal frequency in patients with or without portal vein thrombosis.

Using univariate analysis, the researchers showed that portal vein thrombosis was associated with Child-Pugh classes B and C, and signs of liver decompensation.

The team also showed that portal vein thrombosis was associated with large varices with red markings, sclerotherapy, and abdominal surgery.

The team noted after multivariate analysis, that portal vein thrombosis was associated with sclerotherapy and previous surgery.

The researchers observed that combination of the 2 acquired factors increased risk for portal vein thrombosis, whereas combination of local with genetic defects did not.

The team reported that only 1 patient with genetic thrombophilia and without portal vein thrombosis at inclusion developed the complication during follow-up.

The 1 patient who developed complications, concomitantly developed hepatocellular carcinoma.

Dr Mangia concludes, "In cirrhotic patients prothrombotic mutations by themselves are not causative of portal vein thrombosis."

"Sclerotherapy and previous abdominal surgery favour the development of two-thirds of cases of portal vein thrombosis; in the remaining cases the pathogenesis remains elusive."

Eur J Gastroenterol & Hepatol 2005: 17(7): 745-51

June 17th, 2005

Predictors and Impact of Hepatic Steatosis in Hep B and C

SourceURL: <http://www.gastrohep.com>

Hepatic steatosis is common in chronic Hepatitis B and C showing association with waist circumference, glucose, C-peptide, and chronic Hepatitis C genotype 3, finds July's issue of the *Journal of Hepatology*.

Chronic Hepatitis B and C are commonly associated with hepatic steatosis.

Dr Roberts and colleagues investigated predictors of hepatic steatosis, and their impact on inflammation and fibrosis in chronic Hepatitis B and C.

The researchers included consecutive patients with either chronic Hepatitis B or C who had a liver biopsy at The Alfred Hospital in 2002.

Alcohol intake and age are predictors of hepatic fibrosis – Journal of Hepatology

The histological analysis of liver biopsies was performed by 2 hepatopathologists blinded to the clinical data.

The research team analyzed 91 patients including 17 patients with chronic Hepatitis B and 74 with chronic Hepatitis C.

The team found that chronic Hepatitis C genotype 3, C-peptide, glucose and waist circumference were independent predictors of extent of Brunt steatosis grade.

The team also found that chronic Hepatitis C genotype 3, C-peptide and waist circumference were independent predictors of microvesicular steatosis grade.

The researchers observed that alcohol intake and age were predictors of hepatic fibrosis.

The team identified a trend in correlation between Brunt steatosis and microvesicular steatosis grades, and fibrosis progression rate in chronic Hepatitis C genotype non-3.

Dr Robert's team concludes, "Hepatic steatosis is common in chronic Hepatitis B and C."

"Hepatic steatosis is associated with waist circumference, glucose, C-peptide and chronic Hepatitis C genotype 3."

"Steatosis grade appears to relate to hepatic fibrosis progression rate in chronic Hepatitis C genotype non-3."

June 18th, 2005

Aethlon Medical to Initiate Hepatitis-C Studies

SourceURL: <http://www.investors.com>

San Diego, California -- Aethlon Medical, Inc. (OTCBB:AEMD), a Company pioneering the development of medical devices that mimic the immune response of clearing viruses and toxins from circulation, announced today that it plans to initiate clinical trials to treat patients in India who are infected with the Hepatitis-C Virus (HCV). The Company reported that site selection for the trials is under way, and that patient enrollment should begin in the coming months.

Aethlon CEO, James A. Joyce stated, "This is a tremendous opportunity for us to demonstrate the safety and effectiveness of our HIV-Hemopurifier." Joyce continued, "We are passionate in our efforts to provide a new treatment option to the large population of HCV infected individuals that are unresponsive to the current standard of care."

About Aethlon Medical

Aethlon Medical is developing viral filtration devices to treat HIV/AIDS, Hepatitis-C (HCV), and pathogens that are potential mass casualty biowarfare candidates. Each treatment application employs the use of a proprietary technology known as the Hemopurifier™ which is designed to rapidly reduce the presence of infectious disease and toxins in the body. The Hemopurifier converges the established scientific principals of affinity chromatography and hemodialysis as a means to augment the immune response of clearing viruses and toxins from the blood before cell and organ infection can occur. More information on Aethlon Medical and the Hemopurifier technology is available at www.aethlonmedical.com.

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