










HCV ADVOCATE WEEKLY NEWS REVIEW

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

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May 24th, 2004

Rigel Initiates Phase I/II Trial of R803 For The Treatment Of Hepatitis C Virus

Source: PRNewsire

Hepatitis C Virus Affects an Estimated 170 Million People Worldwide, with Three to Four Million New Infections Every Year

SOUTH SAN FRANCISCO, Calif. -- Rigel Pharmaceuticals, Inc. (Nasdaq: RIGL) today announced the initiation of a multi-dose Phase I/II clinical trial for R803, an experimental drug to treat the blood-borne liver disease Hepatitis C Virus (HCV). The goals of this trial are to assess safety, tolerability and pharmacokinetics of multiple dose administrations of R803 in patients with HCV. The trial will also explore the effectiveness of various dosing regimens of R803 in reducing viral levels. Results of this trial are expected by the fourth quarter of 2004 and will allow Rigel to enter into the broader, longer-term trials, which are necessary for FDA approval.

The Phase I/II multi-dose clinical trial is a double-blind, placebo- controlled, dose-ascending study in subjects with diagnosed HCV. There will be eight groups of subjects, with each subsequent group receiving an increasing dose or increasing number of days of treatment. Subjects will be dosed for two to four days, plus the morning dose on the following day. In January, Rigel released the results of a Phase I clinical trial, which evaluated the safety of R803

in healthy volunteers. No clinically adverse effects were attributed to R803 during this trial at relevant dose levels.

"HCV is a serious global epidemic, and since the current therapies have significant limitations, new therapies are needed to treat this infection," commented Elliott B. Grossbard, M.D., Senior Vice President, Medical Development of Rigel. "Rigel's R803 represents a novel approach in the treatment of HCV, and is one of the first direct antiviral agents to reach human clinical trials."

"Because of its unique mechanism of action, Rigel's R803 has great promise as a potential therapeutic in the fight against HCV," noted Donald G. Payan, M.D., Chief Scientific Officer and Executive Vice President of Rigel. "Rigel is committed to the development of this compound and to furthering treatment options for those affected by HCV."

Rigel's R803, a non-nucleoside HCV polymerase inhibitor, is an oral, small-molecule compound. To date, R803 has demonstrated potent efficacy in inhibiting viral replication in cell-based assay systems and in live virus assays. In these models, R803 has been shown to be active against various genotypes of HCV, including genotype 1, the most common in North America and Europe. In various assays, R803 appears to act within days to reduce viral levels significantly. In addition, as a result of R803's novel viral binding site, resistance may be slow to develop. In cell-based systems, R803 has demonstrated synergy when used with interferon alpha (IFN). This observation may allow the use of a reduced dose of IFN, potentially minimizing the significant side effects of that drug.

HCV: Current Treatments and Market Opportunity

Hepatitis C is an inflammation of the liver caused by HCV. As the most common blood-borne infection in the U.S., HCV affects approximately 4 million Americans and 170 million individuals worldwide. Approximately 80 percent of those with acute illness will go on to develop chronic hepatitis, a condition that has been linked to cirrhosis, hepatocellular carcinoma (liver cancer) and liver failure. HCV accounts for 30 percent of end-stage liver disease and liver cancer and is the leading cause of liver failure, which can result in the need for liver transplantation. Public health officials in the U.S. and abroad have mobilized to address this medical crisis by identifying detection guidelines for HCV and implementing therapies to eradicate chronic infection.

Currently available HCV therapies are only modestly effective at treating the disease. The most prevalent treatment regimen utilizes IFN, usually in combination with ribavirin. IFN shows only a 20 to 40 percent success rate in patients who complete therapy, with significant side effects resulting in up to half the patients either quitting treatment or moving to a lower dose regimen. Moreover, IFN is least effective against HCV genotype 1, the strain responsible for 70 percent of chronic HCV infection cases in the U.S. Rigel believes that its approach is substantially different from that of IFN; instead of working to boost the immune system, experiments indicate that R803 directly, rapidly, selectively and potently targets HCV by interfering with a viral polymerase protein that is needed for replication.

With the current high prevalence and projected increase in cases of HCV and related diseases, and with the limited success of currently available therapies, Rigel believes that the potential for new direct HCV therapeutics is large and that R803 has the potential to be at the forefront of this opportunity.

About Rigel

Rigel's mission is to become a source of novel, small-molecule drugs to address large, unmet medical needs. We have initiated three development programs: asthma/allergy, hepatitis C and rheumatoid arthritis. Rigel has begun clinical testing of its first two product candidates, R112 for allergic rhinitis and R803 for hepatitis C, and expects to begin clinical trials of R406 for the treatment of rheumatoid arthritis by the end of 2004, to be followed by clinical trials for drug candidates in asthma and oncology (www.rigel.com).

This press release contains "forward-looking" statements, including statements related to Rigel's plans to pursue clinical development of product candidates and the timing thereof and the potential efficacy of product candidates. Any statements contained in this press release that are not statements of historical fact may be deemed to be forward-looking statements. Words such as "plans," "intends," "expects" and similar expressions are intended to identify these forward-looking statements. There are a number of important factors that could cause Rigel's results to differ materially from those indicated by these forward-looking statements, including risks associated with the timing and success of clinical trials and the commercialization of product candidates, as well as other risks detailed from time to time in Rigel's SEC reports, including its Annual Report on Form 10-K for the year ended December 31, 2003, and its Quarterly Report on Form 10-Q for the quarter ended March 31, 2004. Rigel does not undertake any obligation to update forward-looking statements.

May 25th, 2004

Hepatitis B Antenatal Screening Program in Amsterdam

Source: www.gastrohep.com

Tracing and immunizing susceptible contacts of women screened for hepatitis B virus, should be an integral part of a control program, find researchers in the June issue of the *Journal of Hepatology*.

Hepatitis B control in Europe concentrates on antenatal screening to reduce vertical transmission.

In an attempt to reduce horizontal transmission and the pool of infectious individuals, the health authorities in Amsterdam integrated the tracing and immunizing of contacts in the antenatal screening program.

In this study, researchers from the Netherlands evaluated this public health program between 1992 and 1999.

In the program, all contacts are tested for serological markers of previous infection. Vaccination is offered to susceptible contacts.

In addition, chronically infected contacts are counseled and referred for treatment if justified. 94% of contacts completed the vaccination series.

Journal of Hepatology

Overall, the researchers found that for 738 women testing positive for the hepatitis B surface antigen, 1219 contacts were reported.

Of the 1219 contacts, 90% participated. The team found that 43% had serological markers of previous infection and of these, 25% were infectious.

There were 603 eligible contacts. Of these, 94% completed the vaccination series.

The research team determined that country of origin was an independent predictor of contact participation and compliance with completion of the vaccination series.

They found that postvaccination titers for antibodies against the surface antigen were below 10IU/L in 5% of contacts under 30 and in 12% of those over 30.

Dr Jim van Steenberg and colleagues concluded, "Tracing and immunizing susceptible contacts of women screened as HBsAg-positive, should be an integral component of any country's HBV control program".

J Hepatol 2004; 40(6): 979-85

Vertex Pharmaceuticals Announces Plans for the METRO Study: Triple Combination of Merimepodib, Pegasys(R) and Copegus(R) in Hepatitis C Patients

Source: PRNewswire

-- Roche Agrees to Provide Pegasys and Copegus for Phase Iib Clinical Trial --

Cambridge, Mass.-- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) announced today the design of a Phase Iib clinical study that it plans to conduct with merimepodib, an investigational oral therapy for the treatment of hepatitis C virus (HCV) infection, in patients who are non-responders to prior treatment with pegylated interferon (peg-IFN) and ribavirin. The clinical trial will be conducted at centers in the United

States and is expected to enroll approximately 315 patients who will receive merimepodib or placebo in combination with Pegasys(R) (peginterferon alfa-2a) and Copegus(R) (ribavirin). Roche will provide Pegasys and Copegus to Vertex for use in this study, providing support for the clinical development of merimepodib as an investigational agent that may enhance the antiviral activity of Pegasys and Copegus, which is the most frequently prescribed treatment combination for HCV infection in the United States. As part of the supply agreement with Roche, Vertex will share data and data analysis with Roche at predetermined intervals during the course of the study. Vertex owns worldwide development and commercialization rights to merimepodib.

"HCV-infected patients who do not respond to initial combination therapy with pegylated interferon plus ribavirin face limited treatment options and the prospect of worsening liver disease," stated John J. Alam, M.D., Senior Vice President of Drug Evaluation and Approval at Vertex. "Preclinical and clinical data reported to date for merimepodib, Vertex's lead oral therapy for HCV infection, have highlighted the potential for this drug candidate to enhance the standard of care in hepatitis C. In this Phase Iib clinical trial, we will seek to evaluate the ability of a triple combination of merimepodib plus peginterferon alfa-2a and ribavirin to increase viral clearance in patients who are refractory to prior combination treatment."

Merimepodib Triple Combination Study (The METRO Study)

The Merimepodib Triple Combination study (the METRO study) has been designed as a double-blind, placebo-controlled, randomized Phase IIb study, with a goal of evaluating the antiviral activity of two doses of merimepodib (MMPD) in combination with Pegasys and Copegus. Vertex anticipates that the trial will enroll approximately 315 patients who were previously non-responders to combination therapy, defined as at least 12 weeks of prior pegylated interferon-alfa and ribavirin treatment without having achieved undetectable HCV-RNA (< 50 I.U.) at any timepoint. The trial is designed so that patients will be treated with 50 mg MMPD, 100 mg MMPD, or placebo twice daily in combination with standard doses of Pegasys and Copegus for an initial period of 24 weeks. At the end of 24 weeks, patients with undetectable HCV-RNA will receive combination therapy with Pegasys and Copegus, only, for an additional 24 weeks. Patients completing the 48-week treatment period will be followed for an additional 24-week treatment-free period. The study is expected to involve more than 40 clinical centers and will be conducted in the United States. Study site selection is underway, and the first centers are expected to begin enrolling patients in the third quarter of 2004.

The goal of the METRO study will be to evaluate the safety, pharmacokinetics and efficacy of MMPD in combination with pegylated interferon. The primary endpoint of the study is to evaluate the antiviral activity of MMPD and perform an assessment of the proportion of MMPD-treated patients who achieved a sustained virologic response (SVR) compared to placebo at week 72 (end of follow-up). Secondary endpoints include evaluation of the antiviral activity of MMPD-treated patients at 12, 24, and 48 weeks. The doses and duration of MMPD treatment in this study have been selected based on comprehensive analysis of the relationship between plasma exposure and antiviral effect in previous clinical studies of merimepodib, as well observations from previous clinical studies that suggest that merimepodib enhances the antiviral activity of combination therapy primarily in the first 24 weeks of treatment.

About Merimepodib and HCV

Merimepodib is a small molecule, orally administered inhibitor of the enzyme inosine monophosphate dehydrogenase (IMPDH). IMPDH inhibition leads to a reduction in intracellular guanosine triphosphate (GTP), a molecule required for DNA and RNA synthesis. Six-month results from a Phase II study presented at the Annual Meeting for the European Association for the Study of the Liver (EASL) demonstrated that relative to placebo treatment, merimepodib treatment produced a statistically significant, dose-dependent increase in the percentage of treatment-refractory patients with HCV genotype 1 who achieved undetectable levels of HCV-RNA at six months. Recent reports in the medical literature suggest that IMPDH inhibitors such as merimepodib may enhance the antiviral activity of ribavirin in vitro by depleting GTP and increasing the rate of incorporation of ribavirin into viral RNA, rendering the virus nonfunctional. The antiviral activity observed clinically when merimepodib is added to ribavirin-containing HCV therapies is consistent with these preclinical findings. In combination with the standard of care, MMPD may help to increase the sustained viral response rate in HCV patients, the principal goal of treatment.

Chronic hepatitis C virus (HCV) infection is a serious public health concern affecting approximately 2.7 million people in the United States. HCV causes inflammation of the liver, which may lead to fibrosis and cirrhosis, liver cancer, and ultimately, liver failure. Cirrhosis of the liver resulting from chronic HCV infection is the leading indication for liver transplantation in the U.S. Due to the asymptomatic nature of HCV infection, it often goes undetected for up to

20 years following initial infection. Worldwide, the disease strikes as many as 185 million people. Each year, 8,000 to 10,000 people in the U.S. die from complications of HCV.

About Vertex

Vertex Pharmaceuticals Incorporated is a global biotechnology company committed to the discovery and development of breakthrough small molecule drugs for serious diseases. The Company's strategy is to commercialize its products both independently and in collaboration with major pharmaceutical partners. Vertex's product pipeline is principally focused on viral diseases, inflammation, autoimmune diseases and cancer.

About Roche

Headquartered in Basel, Switzerland, Roche is one of the world's leading innovation-driven healthcare groups. Its core businesses are pharmaceuticals and diagnostics. Roche is number one in the global diagnostics market, the leading supplier of pharmaceuticals for cancer and a leader in virology and transplantation. As a supplier of products and services for the prevention, diagnosis and treatment of disease, the Group contributes on a broad range of fronts to improving people's health and quality of life. Roche employs roughly 62,000 people in 150 countries. The Group has alliances and research and development agreements with numerous partners, including majority ownership interests in Genentech and Chugai.

This press release may contain forward-looking statements, including statements that (i) merimepodib holds promise as part of combination therapy for HCV patients who have limited treatment options and represents an attractive commercial opportunity for Vertex; and (ii) a Phase IIb clinical study of merimepodib will be initiated in the second half of 2004. While management makes its best efforts to be accurate in making forward-looking statements, such statements are subject to risks and uncertainties that could cause Vertex's actual results to vary materially. These risks and uncertainties include, among other things, the risks that clinical trials for merimepodib may not be initiated or, if initiated, may not proceed as planned due to technical, scientific, or patient enrollment issues, that results from planned clinical trials with merimepodib will not reflect the positive results from earlier trials, that positive nonclinical study results for merimepodib will not be duplicated in future nonclinical or clinical studies and other risks listed under Risk Factors in Vertex's form 10-K filed with the Securities and Exchange Commission on March 15, 2004.

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Vertex's press releases are available at www.vrtx.com.

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(VRTX)

Newly Published Study Investigates Pegasys (peginterferon alfa-2a) and Copegus (ribavirin, USP) for the Treatment of Chronic Hepatitis C In Black Americans

Source: Company Press Release

Authors state: "To date, this is the highest response rate to treatment observed in a black population" -

New York, NY – A study published in the June issue of *Hepatology* showed that 26 percent of black Americans with chronic hepatitis C treated with the most prescribed hepatitis C therapy in the U.S., a combination of Pegasys (peginterferon alfa-2a), a pegylated interferon, and Copegus (ribavirin, USP), an anti-viral medication, achieved a sustained virological response (SVR).

Sustained virological response refers to a patient's continued undetectable serum hepatitis C RNA levels 24 weeks after finishing a course of treatment. The primary objective of the study was to investigate the efficacy, safety and tolerability of Pegasys combination therapy in non-Hispanic black Americans with genotype 1 hepatitis C virus (HCV), the strain of the virus that is most difficult to treat. In the article, the authors of the study state: "In summary, we have shown that 48 weeks of therapy with peginterferon alfa-2a and ribavirin results in an SVR in 26 percent of blacks chronically infected with HCV genotype 1. To date, this is the highest response rate to treatment observed in a black population." In black patients who completed 48 weeks of treatment, 32 percent achieved an SVR.

"Historically, black Americans infected with hepatitis C have been underrepresented in clinical trials," said Lennox Jeffers, MD, professor of medicine at the University of Miami School of Medicine and chief of Hepatology at the Miami VA Medical Center. "These results are very encouraging and have already led to a large National Institutes of Health (NIH) study involving 400 patients in eight centers throughout the United States to examine viral hepatitis C resistance in the black American population."

Hepatitis C is a blood-borne virus that chronically infects an estimated 2.7 million Americans. It can cause progressive liver injury and lead to fibrosis and eventually cirrhosis. Black Americans have the highest prevalence rates for hepatitis C among all racial and ethnic groups in the U.S. and hepatitis C treatment has historically been less effective in this population.

"The results of this study provide promising information for black Americans infected with hepatitis C," said Charles Howell, MD, associate professor in the Department of Medicine and director of Hepatology Research at the University of Maryland School of Medicine, and one of the lead investigators in the study. "Until now, the efficacy of peginterferon plus ribavirin for hepatitis C treatment in black Americans was unclear. This new data establishes the efficacy and safety of peginterferon alfa-2a (Pegasys) and ribavirin for African Americans infected with genotype 1, the most common variant of hepatitis C in the United States."

Study Design

The open-label noncomparative study was conducted at eleven sites in the United States and included 78 black patients and 28 white patients.

All patients were interferon-naïve with chronic hepatitis C genotype 1 and elevated ALT levels. Patients received 180 mcg subcutaneously of Pegasys, once weekly, along with either 1000 or 1200 mg/day of Copegus, depending on their weight, for 48 weeks, with 24 weeks of treatment-free follow-up. Early virological response (EVR) was assessed at 12 weeks of therapy and SVR at week 72.

This trial included a relatively small cohort of patients receiving treatment. Studies with larger patient populations are currently underway to confirm the findings from this study.

The SVR rate in white patients in the study was 39 percent, with a confidence interval of 21 to 57 percent. Conclusions should not be drawn in the white patient population because of the small number (n=28) in the study. In previous studies, more than half of patients with genotype 1 hepatitis C achieved a sustained virological response after 48 weeks of treatment with Pegasys combination therapy.

Histological Response

Paired liver biopsies were obtained from 53 of the black patients and 16 of the white patients. In these patients, more than 90 percent in both groups showed either improvement or stabilization of fibrosis (scar tissue in the liver). Improvements in fibrosis score occurred in 25 percent of all patients (13 of 53 patients).

Adverse Events

Adverse events were similar to those seen in Pegasys and Copegus registration trials. Incidence rates for AEs among the white patient and black patient groups included: fatigue (71 percent vs. 60 percent), headache (82 percent vs. 54 percent), rigors (35 percent vs. 32 percent), insomnia (50 percent vs. 27 percent), rash (26 percent vs. 18 percent), and nausea (54 percent vs. 23 percent). Five percent of black patients and fourteen percent of white patients withdrew prematurely due to adverse events or laboratory abnormalities. Black patients had lower baseline absolute neutrophil counts compared to white patients. Dose modifications of Pegasys (withheld or reduced) occurred among 46 percent of black patients and 29 percent of white patients; the most common cause was neutropenia (37 percent among black patients and 18 percent among white patients).

About Pegasys

Pegasys, a pegylated alpha interferon, and Copegus, an oral antiviral, were approved by the FDA in December 2002 for use in combination for the treatment of adults with chronic hepatitis C who have compensated liver disease and have not previously been treated with interferon alpha. Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis.

About Roche

Hoffmann-La Roche Inc. (Roche), based in Nutley, N.J., is the U.S. prescription drug unit of the Roche Group, a leading research-based health care enterprise that ranks among the world's leaders in pharmaceuticals, diagnostics and vitamins. Roche discovers, develops, manufactures and markets numerous important prescription drugs that enhance people's health, well-being and

quality of life. Among the company's areas of therapeutic interest are: dermatology; genitourinary disease; infectious diseases, including influenza; inflammation, including arthritis and osteoporosis; metabolic diseases, including obesity and diabetes; neurology; oncology; transplantation; vascular diseases; and virology, including HIV/AIDS and hepatitis C. For more information on the Roche pharmaceuticals business in the United States, visit the company's web site at: <http://www.rocheusa.com>

African-Americans Respond Poorly to Hepatitis C Treatment

Duke University Medical Center

Durham, N.C. - African-Americans have a significantly lower response rate to treatment for chronic hepatitis C than non-Hispanic whites, according to a new study led by Duke University Medical Center researchers.

Some African-Americans - 19 percent - did respond to the drug combination of peginterferon alfa-2b and ribavirin. But in non-Hispanic whites with the same disease, the hepatitis C genotype 1 virus strain, 52 percent had no evidence of the virus in their blood six months after completing the drug therapy - one of the highest response rates ever reported for this therapy.

The study showed the difference in infection rates between the two groups is not responsible for the low response rate to treatment in African-Americans.

"This study definitively proves that the difference in response rate is not due to the higher rate of genotype 1 infection in African-Americans," said Andrew Muir, M.D., lead author of the study and an assistant professor of medicine at Duke University Medical Center. The results were published May 27, 2004, in the *New England Journal of Medicine*.

Muir recommends African-Americans consult their physicians about the decision to receive treatment for hepatitis C.

"These results should be discussed with African-American patients with hepatitis C. However, we must also let patients know that some African-Americans did respond to therapy, and African-American patients should continue to be considered for treatment," said Muir, a gastroenterologist.

The prospective study followed 100 African-American and 100 non-Hispanic white chronic hepatitis C patients during 48 weeks of drug treatment. The majority of both patient groups, 98 percent, had hepatitis C genotype 1, which has a lower response rate to treatment than other hepatitis C genotypes. This virus strain is the most common form of the hepatitis C in the United States and is the most difficult to treat, Muir said. An estimated 4 million people in the United States are infected with hepatitis C.

African-Americans have a higher rate of genotype 1 infection than non-Hispanic whites. Earlier studies had suggested the prevalence of genotype 1 infection in African-Americans was responsible for their lower response rate to treatment, because the virus strain is difficult to treat.

By comparing similar patient groups, the researchers determined that the difference in infection rates does not explain the lower response rate to treatment among African-Americans.

Statistical analyses of characteristics such as sex, age, weight, level of education, duration of infection and other medical conditions showed race was the only variable associated with a significant difference in response to treatment. In addition, side effects and tolerance of the medications were similar in both groups.

"The reasons for the lower response in African Americans are still unclear. We need further research to better understand the reason for the lower response rate," Muir said.

Patients were drawn from the community and seen in clinical practice by members of the Atlantic Coast Hepatitis Treatment Group, which includes 16 centers in North Carolina, South Carolina, Virginia and Tennessee. The baseline characteristics of both groups were similar. The study was supported by Schering-Plough, manufacturer of the drug combination therapy.

The drug treatment goal was a sustained virologic response, which means the patient has no detectable hepatitis C virus in blood tests six months after treatment ends. Both groups were treated with peginterferon alfa-2b and ribavirin. Peginterferon is an injectable, long-acting form of interferon, a synthetic version of immune system substance produced by the body to help fight infections. Patients received a dose of peginterferon alfa-2b every week. Ribavirin is an oral antiviral drug; patients took the drug every day in pill form.

Muir has received an American Association for the Study of Liver Diseases/Schering-Plough Advanced Hepatology Fellowship. He has also received grant support from Schering-Plough and has served as a paid speaker for Schering-Plough.

May 26th, 2004

Anadys Pharmaceuticals Announces Selection of ANA975 As A Development Candidate For Front-Line Treatment Of Chronic Hepatitis C

Source: Business Wire

Anadys Designates ANA975, an Oral Prodrug of Isatoribine

San Diego-- Anadys Pharmaceuticals, Inc. (Nasdaq:ANDS) today announced it has selected ANA975, an oral prodrug of isatoribine (ANA245), to be its development candidate for front-line treatment of chronic hepatitis C virus (HCV) infection. ANA975 builds from Anadys' clinical experience with isatoribine, including knowledge of isatoribine doses that have been shown to be well-tolerated in Phase 1A and Phase 1B trials and that demonstrated a statistically significant reduction of HCV viral load. Anadys expects that this knowledge will facilitate an accelerated and efficient clinical development program for ANA975.

"ANA975 was selected from the ANA97X family of isatoribine prodrug compounds based upon its favorable pharmaceutical properties, which we believe should allow it to become an orally administered front-line treatment for chronic HCV," said Devron Averett, Ph.D., Senior Vice President of Drug Development for Anadys.

ANA975 is an oral prodrug of isatoribine. Prodrugs are distinct chemical entities that are administered as a precursor of the active drug and then are converted into the active drug in the

body. Isatoribine and its prodrugs are a new class of drugs being developed by Anadys to regulate innate immunity, the body's first line of defense against viruses and other foreign organisms. Anadys believes that isatoribine interacts with a specific receptor on certain immune system cells named TLR-7, which assists in regulating innate immune responses against viruses.

Interim results from a Phase IB clinical trial showed isatoribine to be safe and well-tolerated at all doses tested. Although long term therapeutic utility was not a stated objective of the Phase IB clinical trial, at the 800 mg dose level the viral load difference between the beginning and end of treatment was statistically significant ($p=0.03$), with a median change in viral load from baseline of $-0.94 \log_{10}$ units. Anadys is encouraged by these early results, and believes they provide proof of concept that a compound interacting with TLR-7 can reduce viral load in HCV infected patients.

"We are very pleased in achieving one of our goals for the second quarter of 2004, by selecting a front-line clinical candidate for the treatment of chronic hepatitis C virus infection," said Kleanthis G. Xanthopoulos, Ph.D., President and CEO of Anadys.

"ANA975 broadens our existing pipeline of anti-infective drug candidates, which includes isatoribine and ANA971 for the treatment of HCV, ANA380 for the treatment of hepatitis B virus, and preclinical candidates to treat bacterial infections. We look forward to advancing ANA975 into the clinic."

About isatoribine (ANA245)

Isatoribine is a nucleoside analog Anadys is evaluating in ongoing clinical trials for the treatment of HCV infections. Isatoribine represents one of a new class of drugs being developed by Anadys to regulate innate immunity, combat HCV infection, and overcome limitations of current anti-HCV therapies. Anadys believes isatoribine interacts with a specific receptor, Toll-like receptor 7, or TLR-7, that is present on certain immune system cells. Although results of initial clinical trials may not be predictive of future results, interim results of the Phase IB clinical trial show that isatoribine is biologically active in adults with chronic HCV infection and results from dosing a cohort of six HCV infected patients with 800mg of isatoribine showed a statistically significant reduction of viral load ($p=0.03$) at the end of one week, with a median change in viral load from baseline of $-0.94 \log_{10}$ units. Anadys is currently recruiting patients for an isatoribine Phase I/II study.

About hepatitis C

Hepatitis C virus, the most common chronic blood-borne infection in the United States, causes inflammation of the liver and may progress to more serious complications such as cirrhosis of the liver, liver cancer and death. Approximately 2.7 million people in the United States are chronically infected with HCV, and the Centers for Disease Control (CDC) estimates that by the year 2010, the number of deaths attributed annually to HCV could surpass that due to HIV/AIDS. Worldwide sales for anti-infective products were \$40 billion in 2002, yet current treatments for HCV may be ineffective in up to 50% of patients due to the development of drug-resistant viral strains, and many treatments are associated with serious side effects.

About Anadys Pharmaceuticals, Inc.

Anadys Pharmaceuticals, Inc. (www.anadyspharma.com) is a biopharmaceutical company committed to advancing patient care by discovering, developing and commercializing novel small molecule, anti-infective medicines for the treatment of hepatitis C virus, hepatitis B virus and

bacterial infections. Anadys is advancing its anti-infective portfolio through the development of its two clinical programs, the isatoribine family of compounds and ANA380. In addition, Anadys' anti-infective therapeutic platform is designed to advance a strong and continual pipeline of drug candidates into the clinic.

Safe Harbor Statement

Statements in this press release that are not strictly historical in nature constitute "forward-looking statements." Such statements include, but are not limited to, references to the biological activity of isatoribine in HCV infected patients, viral load reduction resulting from administration of isatoribine to HCV infected patients, the believed mechanism of action of isatoribine and its effect on a patient's immune system, the favorable pharmaceutical properties of ANA975, the potential for ANA975 to become an orally administered front-line treatment for chronic HCV and expectations regarding the timing and duration of further clinical trials of isatoribine and ANA975. Such forward-looking statements involve known and unknown risks, uncertainties and other factors which may cause the actual results of Anadys Pharmaceuticals to be materially different from historical results or from any results expressed or implied by such forward-looking statements. In particular, the results of initial clinical trials are not necessarily predictive of future results, and Anadys can provide no assurances that isatoribine or ANA975 will have favorable safety, tolerability or efficacy results in later clinical trials, or receive regulatory approval. In addition, Anadys' results may be affected by competition from other biotechnology and pharmaceutical companies, its effectiveness at managing its financial resources, its ability to successfully develop and market products, difficulties or delays in its clinical trials, difficulties or delays in manufacturing its clinical trials materials, the scope and validity of patent protection for its products, regulatory developments involving future products and its ability to obtain additional funding to support its operations. These and other factors that may cause actual results to differ are more fully discussed in the "Risk Factors" section of Anadys' Form 10-Q for the quarter ended March 31, 2004. All forward-looking statements are qualified in their entirety by this cautionary statement. Anadys is providing this information as of this date and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

SciClone Announces Collaboration To Develop Pegylated Zadaxin

Source: Business Wire

San Mateo, CA --SciClone Pharmaceuticals, Inc. (Nasdaq:SCLN) today announced that it has entered into a collaborative agreement with Nektar Therapeutics' (Nasdaq:NKTR) subsidiary, Nektar Therapeutics, AL Corporation to develop a pegylated formulation of ZADAXIN(R). Nektar will apply its Advanced PEGylation technology to ZADAXIN with the objective of improving the therapeutic use and potential efficacy of the compound. SciClone has filed for worldwide patent protection for the composition-of-matter of pegylated ZADAXIN.

Dr. Cynthia Tuthill, Vice President of Scientific Affairs at SciClone commented, "We are very pleased to be working with Nektar, a recognized leader in the field of pegylation technology, on this significant initiative." If the formulation is successful, pegylated ZADAXIN could lead to improved patient compliance due to less frequent dosing and would allow the drug to remain in the body at a higher concentration level for a longer period of time. In addition to potentially enhancing the use of ZADAXIN in the treatment of hepatitis C and hepatitis B, SciClone believes that a pegylated formulation also could broaden the potential application of ZADAXIN in cancer therapy.

About Nektar Advanced PEGylation

Nektar Advanced PEGylation, developed by Shearwater, now part of Nektar, is based on the use of non-toxic polyethylene glycol (PEG) polymers, which can be attached to most major drug classes, including proteins, peptides, antibody fragments, small molecules, and other drugs. Nektar Advanced PEGylation has the potential to improve the safety and efficacy of therapeutic agents by increasing drug circulation time in the bloodstream, increasing bioavailability, decreasing immunogenicity, decreasing dosing frequency, and improving drug solubility and stability.

About SciClone

SciClone Pharmaceuticals is a biopharmaceutical company engaged in the development of therapeutics to treat life-threatening diseases. SciClone is currently evaluating its lead product ZADAXIN in several clinical trials, including two phase 3 hepatitis C clinical trials in the U.S., a completed phase 3 hepatitis B clinical trial in Japan, a phase 2 malignant melanoma clinical trial in Europe, two phase 2 liver cancer pilot studies in the U.S., a hepatitis C triple therapy open-label clinical trial in Mexico, and a hepatitis B combination therapy trial in Taiwan. SciClone recently announced plans for a ZADAXIN phase 3 hepatitis C triple therapy clinical trial in Europe. The Company's other principal drug development candidate is SCV-07, a potentially orally available therapeutic to treat viral and infectious diseases. For more information about SciClone, visit www.sciclone.com.

About Nektar Therapeutics

Nektar Therapeutics provides industry-leading drug delivery technologies, expertise and manufacturing to enable the development of high-value, differentiated therapeutics. Nektar's advanced drug delivery capabilities are designed to enable the company's biotechnology and pharmaceutical partners to solve drug development challenges and realize the full potential of their therapeutics, from developing new molecular entities to managing the life cycles of established products.

Human Genome Sciences Initiates Phase 2 Clinical Trial Of Albuferon(TM) For The Treatment Of Chronic Hepatitis C

Source: PRNewswire

Rockville, MD -- Human Genome Sciences, Inc. (Nasdaq: HGSI) announced today that it has begun dosing patients in a Phase 2 clinical trial of Albuferon(TM) (albumin-interferon alpha) in patients with chronic hepatitis C who are naive to interferon-alpha treatments.

The Phase 2 trial is a randomized, open-label, multi-center, parallel- design dose-ranging study to evaluate the safety, tolerability, pharmacology, and optimal dosing of Albuferon.

The Phase 2 clinical trial will be conducted in Canada, and will enroll approximately forty patients with hepatitis C virus (HCV) genotype 1. Genotype 1 accounts for nearly seventy percent of all HCV infections in North America and is generally regarded as the most difficult HCV genotype to treat. A minimum of ten patients will be randomized to each of three dose groups, which will be given two doses of Albuferon administered subcutaneously fourteen days apart. The pharmacodynamic activity of Albuferon will be evaluated based on HCV RNA viral load reductions over a 28-day period of exposure and early virologic response at Day 28. One of the study objectives is to identify a range of active doses that Human Genome Sciences plans to

evaluate in a larger 48-week study of Albuferon in combination with ribavirin in patients with HCV genotype 1 who are naive to interferon treatments.

Interim results of an ongoing Phase 1/2 clinical trial of Albuferon in interferon-experienced adults with chronic hepatitis C were presented at the April 2004 Annual Meeting of the European Association for the Study of the Liver (EASL) in Berlin.(1) Interim results demonstrate that Albuferon is well tolerated, has a prolonged half-life, and is biologically active. On average, patients participating in the ongoing clinical trial had been treated previously for approximately 68 weeks with regimens containing interferon alpha or pegylated interferon. Data were presented at the EASL meeting on fifty-one patients who were enrolled under an amendment to the original protocol and were treated with single doses of Albuferon administered subcutaneously at 120 micrograms (mcg), 180 mcg, 240 mcg, 320 mcg, 400 mcg, 500 mcg, or 600 mcg -- or with two doses of Albuferon administered subcutaneously fourteen days apart at 400 mcg or 500 mcg. All cohorts treated under the amended protocol showed evidence of biological activity. Viral load levels represent the quantity of hepatitis C virus in the blood, and reductions in viral load are a surrogate marker for clinical benefit. Fifty-five percent (28/51) of Albuferon-treated patients in the combined single-injection and double-injection cohorts experienced an antiviral response, as demonstrated by reductions in their viral load of 0.5 log or greater at two consecutive time points. Of those experiencing an antiviral response, seventy-nine percent (22/28) experienced reductions of at least 0.9 log units.

Vijayan Balan, M.D., a lead investigator and Director, Hepatobiliary Clinic, Division of Transplant Medicine and Division of Gastroenterology and Hepatology, Mayo Clinic Hospital, Phoenix, AZ, said, "Hepatitis C is the most common chronic blood-borne infection in the developed world. It afflicts approximately four million people in the United States alone, about four times the number afflicted by HIV, the virus that causes AIDS. There is a significant need to provide hepatitis C patients with additional treatment options, and Albuferon has looked promising in our initial studies. Further development in interferon-naive patients is warranted."

David C. Stump, M.D., Executive Vice President, Drug Development, said, "Based on the positive interim clinical results that continue to emerge from our ongoing Phase 1/2 clinical trial of Albuferon in patients with chronic hepatitis C, we are pleased to advance Albuferon to a Phase 2 study in patients who are naive to treatments with interferon alpha.(1)(2) We believe that the Phase 2 study will yield important additional information about Albuferon's safety, pharmacology, and biological activity, and also should enable us to identify an optimal range of doses to evaluate in a larger 48-week combination study of Albuferon that we plan to conduct in treatment-naive patients."

Albuferon is a novel, long-acting form of interferon alpha. Recombinant interferon alpha is approved for the treatment of hepatitis C, hepatitis B, and a broad range of cancers. Human Genome Sciences modified interferon alpha to improve its pharmacological properties by using the company's proprietary albumin fusion technology. Human Genome Sciences is developing Albuferon for use in the treatment of chronic hepatitis C.

Hepatitis C infection is an inflammation of the liver caused by the hepatitis C virus. The hepatitis C virus is transmitted primarily through significant or repeated exposures to infected blood. In the United States, intravenous drug use and sexual contact with infected persons account for the majority of new hepatitis C infections. When detectable levels of the hepatitis C virus in the blood persist for at least six months, a person is diagnosed as having chronic hepatitis C. The

current standard of care for treating chronic hepatitis C is combination therapy consisting of pegylated interferon and ribavirin, an antiviral drug.(3)

Health professionals interested in more information about trials involving HGSI products are encouraged to inquire via the Contact Us section of the Human Genome Sciences web site, <http://www.hgsi.com/products/request.html>, or by calling (301) 610-5790, extension 3550.

Human Genome Sciences is a company with the mission to treat and cure disease by bringing new gene-based protein and antibody drugs to patients.

HGS, Human Genome Sciences and Albuferon are trademarks of Human Genome Sciences, Inc.

This announcement contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. The forward-looking statements are based on Human Genome Sciences' current intent, belief and expectations. These statements are not guarantees of future performance and are subject to certain risks and uncertainties that are difficult to predict. Actual results may differ materially from these forward-looking statements because of the Company's unproven business model, its dependence on new technologies, the uncertainty and timing of clinical trials, the Company's ability to develop and commercialize products, its dependence on collaborators for services and revenue, its substantial indebtedness and lease obligations, its changing requirements and costs associated with planned facilities, intense competition, the uncertainty of patent and intellectual property protection, the Company's dependence on key management and key suppliers, the uncertainty of regulation of products, the impact of future alliances or transactions and other risks described in the Company's filings with the Securities and Exchange Commission. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of today's date. Human Genome Sciences undertakes no obligation to update or revise the information contained in this announcement whether as a result of new information, future events or circumstances or otherwise.

Footnotes:

- (1) Balan V, et al. Safety, Pharmacokinetics and Pharmacodynamic Results of Higher Doses of Albuferon(TM) in a Phase 1/2 Single and Double Dose-Escalation Study in Treatment Experienced Subjects with Chronic Hepatitis C. 39th Annual Meeting of the European Association for the Study of the Liver, Berlin. April 15, 2004.
- (2) Balan V, et al. A Phase 1/2 Study to Evaluate the Pharmacokinetics, Safety, Tolerability, Immunogenicity, and Pharmacodynamics of Albuferon(TM)-alpha in Treatment Experienced Subjects with Chronic Hepatitis C. 54th Annual Meeting of the American Association for the Study of Liver Diseases, Boston. October 25, 2003.
- (3) Strader DB, Wright T, Thomas DL, and Seeff, LB. AASLD Practice Guideline: Diagnosis, Management, and Treatment of Hepatitis C. Hepatology 2004 April; 39 (4): 1147-1171.

SOURCE Human Genome Sciences, Inc.

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May 28, 2004

Characteristics and Survival in Hepatocellular Carcinoma

Source: www.gastrohep.com

The characteristics of patients with hepatocellular carcinoma have changed dramatically between 1976 and 1995, find doctors in the latest issue of *Cancer*.

In this study, doctors from Japan analyzed changes in the characteristics and survival rate of patients with hepatocellular carcinoma in the past 25 years.

The team retrospectively evaluated data from 1365 patients with hepatocellular carcinoma who were diagnosed, treated, and followed between 1976 and 2000.

They recorded trends in clinical characteristics and survival rate.

The doctors found that, between 1976 and 1995, the number of patients with smaller tumors, a less advanced tumor stage, and with a lower Child-Pugh class increased.

There were no differences were observed in the distributions of these factors between the periods 1991 and 1995, and 1996 and 2000.

Year of diagnosis contributed independently to improved survival rates.

Cancer

In addition, year of diagnosis, tumor size, tumor stage, Child-Pugh class, and type of initial treatment correlated significantly with patient survival rates.

The year of hepatocellular carcinoma diagnosis was found to contribute to the improvement in patient survival rates.

Dr Hidenori Toyoda and colleagues concluded, "The characteristics of patients with hepatocellular carcinoma changed dramatically from 1976 to 1995 toward the earlier detection of hepatocellular carcinoma".

"This contributed to the improvement noted in patient survival rates during this period".

"The year of hepatocellular carcinoma diagnosis was found to be an independent factor for the improved survival rates by multivariate analysis".

"This indicated that the progress of treatment and care for patients with hepatocellular carcinoma contributed to the annual improvement in patient survival rates".

Cancer 2004; 100(11): 2415-21