



Roche and Pharmasset Initiate Phase IIb Clinical Trial of R7128, Most Advanced Nucleoside Polymerase Inhibitor in Development for Chronic Hepatitis C

--Start of trial triggers \$10 million milestone payment to Pharmasset

PRINCETON, N.J., April 24, 2009 /PRNewswire-FirstCall via COMTEX News Network/ -- Pharmasset, Inc. (Nasdaq: VRUS) and Roche (Roche SWX: RO, ROG; Pink Sheets: RHHBY) today announced that the first patient has been dosed in a Phase IIb study of R7128, the nucleoside polymerase inhibitor most advanced in development for the treatment of chronic hepatitis C (HCV). The trial will evaluate the dose and duration of treatment of R7128 in combination with Roche's PEGASYS(R) (peginterferon alfa-2a) and COPEGUS(R) (ribavirin) - in HCV patients who have not been treated previously. The goal of adding R7128 to the existing standard therapy is to improve rates of sustained virological response (SVR) and to shorten the length of treatment for patients.

R7128 is being developed by Roche and Pharmasset under a partnership agreement entered into in 2004. The first patient dosed in this study triggered a \$10 million payment to Pharmasset from Roche.

A Phase I/IIa trial demonstrated the ability of R7128 to generate high rapid virologic response rates (RVR) in combination with PEGASYS and COPEGUS. Unlike protease inhibitors in development, R7128 is active against multiple HCV genotypes and presents a high barrier to the development of resistance.

"We look for the Phase IIb study to further support the efficacy and safety of R7128, and nucleoside polymerase inhibitors as a class," said Michelle Berrey, MD, MPH, Pharmasset's Chief Medical Officer. "We believe nucleoside inhibitors have a number of advantages over other classes of HCV drugs, including a higher barrier to resistance and activity across multiple genotypes, as well as a high level of potency."

"The collaboration with Pharmasset underscores Roche's commitment to develop new therapies that will meet the needs of a growing population of patients with hepatitis C," said Rob Mitchell, Global Head of Roche's Virology business. "We are hopeful that a combination of R7128 and the current gold standard of PEGASYS and COPEGUS can provide a more potent - and potentially shorter - treatment regimen."

These collaborations position Roche as a leader, and they underscore Roche's role as a pioneer, in the next evolution of hepatology treatments.

About the Phase IIb Trial

The Phase IIb trial is anticipated to enroll about 400 HCV-infected patients with genotypes 1 or 4 who have not been treated previously. The primary efficacy endpoint of the trial will be the proportion of patients who achieve an SVR, defined as undetectable levels of HCV (measured by Roche TaqMan assay) 24 weeks after completion of treatment. The trial will be conducted in North America, Europe and Australia. Patients will be enrolled into one of 5 arms:

- 24 weeks of total treatment, with R7128 500mg bid in combination with PEGASYS and COPEGUS for 12 weeks, followed by 12 weeks of PEGASYS and COPEGUS ("12+12")
- 24 weeks of total treatment, with R7128 1000mg bid in combination with PEGASYS and COPEGUS for 12 weeks, followed by 12 weeks of PEGASYS and COPEGUS ("12+12")
- 24 weeks of total treatment, with R7128 1000mg bid in combination with PEGASYS and COPEGUS for 8 weeks, followed by a further 16 weeks of PEGASYS and COPEGUS ("8+16")
- 48 weeks of total treatment, with R7128 1000mg bid in combination with PEGASYS and COPEGUS for 12 weeks, followed by a further 36 weeks of PEGASYS and COPEGUS ("12+36")
- A control arm with PEGASYS and COPEGUS for 48 weeks.

Patients in the 24-week arms will discontinue all treatment at week 24 if they have achieved RVR, defined as undetectable

levels of HCV at week 4 (a strategy known as "RVR-guided" treatment), and maintain undetectable levels of HCV until week 22. Patients who do not achieve an RVR at week 4 will continue on the standard of care until week 48.

According to the study design, 100 patients will be initially enrolled, equally across all five arms. The remaining 300 will be enrolled following a review of the 12-week data by the data safety monitoring board.

More About R7128

R7128, a cytidine nucleoside analog inhibitor, is being developed for the treatment of chronic HCV infection. R7128 has shown in vitro activity against all of the most common HCV genotypes.

- In a 4-week Phase I combination study conducted in 81 treatment-naive patients with chronic HCV, R7128 demonstrated significant short-term antiviral activity with safety and tolerability comparable to placebo with standard of care. Up to 88 percent of patients achieved undetectable levels of HCV (<15 IU/ml) after only 4 weeks of treatment with R7128 1000mg bid and the standard of care, compared to 18.75 percent treated with the standard of care alone.

- In the harder to treat populations of genotype 2 or 3 patients who had not responded to previous therapy, results with R7127 1500mg twice-daily in combination with the standard of care showed that 90 percent of patients achieved undetectable levels of HCV (<15 IU/ml) after 4 weeks, compared to 60 percent in the standard of care arm.

In November 2008, Roche, Pharmasset and InterMune initiated the INFORM-1 trial to investigate the combination of R7128 with InterMune's R7227, a protease inhibitor, in HCV patients. This is the first-ever clinical study to investigate the combination of two oral antiviral medicines in the absence of weekly injections of interferon, or ribavirin. Interim results of this trial will be presented this weekend at the European Association of Liver Disease (EASL) meeting being held in Copenhagen, Denmark.

About Hepatitis C

The hepatitis C virus (HCV) is transmitted primarily through blood or blood products. HCV chronically affects 180 million people worldwide, which makes it over four times more prevalent than HIV.(i,ii) It is a leading cause of cirrhosis, liver cancer and liver failure.

About Pharmasset

Pharmasset is a clinical-stage pharmaceutical company committed to discovering, developing and commercializing novel drugs to treat viral infections. Pharmasset's primary focus is on the development of oral therapeutics for the treatment of hepatitis C virus (HCV) and human immunodeficiency virus (HIV). Pharmasset is currently developing three product candidates. R7128, an oral treatment for chronic HCV infection, has completed a 4-week clinical trial in combination with PEGASYS plus COPEGUS through a strategic collaboration with Roche, and is initiating a Phase IIb trial. Racivir, which is being developed for the treatment of HIV in combination with other approved HIV drugs, has completed a Phase II clinical trial. PSI-7851, an unpartnered second generation HCV nucleotide analogue recently entered Phase I studies.

Pharmasset Forward-Looking Statements

Pharmasset "Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995: Statements in this press release regarding our business that are not historical facts are "forward-looking statements" that involve risks and uncertainties, including without limitation, the risk that adverse events could cause the cessation or delay of any of the ongoing or planned clinical trials and/or our development of our product candidates, the risk that the results of previously conducted studies involving our product candidates will not be repeated or observed in ongoing or future studies involving our product candidates, the risk that our collaboration with Roche will not continue or will not be successful and the risk that any one or more of our product candidates will not be successfully developed and commercialized. For a discussion of these risks and uncertainties, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section of our Annual Report on Form 10-K for the fiscal year ended September 30, 2008 and our Quarterly Report on Form 10-Q for the period ended December 31, 2008 filed with the Securities and Exchange Commission entitled "Risk Factors" and discussions of potential risks and uncertainties in our subsequent filings with the Securities and Exchange Commission.

About PEGASYS

Combination therapy of pegylated interferon and ribavirin is the current standard of care for the hepatitis C virus (HCV), and PEGASYS is the U.S. and global market-leading treatment for this disease. PEGASYS is also the pegylated interferon therapy of choice for most HCV antiviral agents in development.

PEGASYS, in combination with COPEGUS (ribavirin), is indicated for the treatment of adults with chronic HCV who have compensated liver disease and have not previously been treated with interferon alpha. Efficacy has been demonstrated in patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with HIV disease that are clinically stable (e.g., antiretroviral therapy not required or receiving stable antiretroviral therapy). In addition, PEGASYS in combination with COPEGUS is the first and only FDA-approved regimen for the treatment of chronic HCV in patients coinfecting with HCV and HIV. PEGASYS is the only pegylated interferon indicated for the treatment of adult patients with chronic hepatitis B (HBeAg positive and HBeAg negative chronic hepatitis B who have compensated liver disease and evidence of viral replication and liver inflammation).

PEGASYS is dosed at 180mcg as a subcutaneous injection taken once a week. COPEGUS is available as a 200mg tablet, and is administered orally two times a day as a split dose. Roche has backed PEGASYS with the most extensive clinical research program ever undertaken in HCV, with major studies initiated to advance treatment for HCV patients with unmet needs, including patients co-infected with HIV and HCV, African Americans, patients with cirrhosis, and patients who have failed to respond to previous therapy.

IMPORTANT SAFETY INFORMATION

PEGASYS, alone or in combination with COPEGUS, is indicated for the treatment of adults with chronic hepatitis C virus infection who have compensated liver disease and have not been previously treated with interferon alpha. Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A).

Alpha interferons, including PEGASYS(R) (Peginterferon alfa-2a), may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Therapy should be withdrawn in patients with persistently severe or worsening signs or symptoms of these conditions. In many, but not all cases, these disorders resolve after stopping PEGASYS therapy (see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS and ADVERSE REACTIONS in complete product information).

Use with Ribavirin. Ribavirin, including COPEGUS(R), may cause birth defects and/or death of the fetus. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients. Ribavirin causes hemolytic anemia. The anemia associated with ribavirin therapy may result in a worsening of cardiac disease. Ribavirin is genotoxic and mutagenic and should be considered a potential carcinogen (see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS and ADVERSE REACTIONS in complete product information).

PEGASYS is contraindicated in patients with hypersensitivity to PEGASYS or any of its components, autoimmune hepatitis, and hepatic decompensation (Child-Pugh score greater than 6; class B and C) in cirrhotic CHC monoinfected patients before or during treatment. PEGASYS is also contraindicated in hepatic decompensation with Child-Pugh score greater than or equal to 6 in cirrhotic CHC patients coinfecting with HIV before or during treatment. PEGASYS is also contraindicated in neonates and infants because it contains benzyl alcohol. Benzyl alcohol is associated with an increased incidence of neurological and other complications in neonates and infants, which are sometimes fatal. PEGASYS and COPEGUS therapy is additionally contraindicated in patients with a hypersensitivity to COPEGUS or any of its components, in women who are pregnant, men whose female partners are pregnant, and patients with hemoglobinopathies (eg, thalassemia major, sickle-cell anemia).

COPEGUS THERAPY SHOULD NOT BE STARTED UNLESS A REPORT OF A NEGATIVE PREGNANCY TEST HAS BEEN OBTAINED IMMEDIATELY PRIOR TO INITIATION OF THERAPY. Women of childbearing potential and men must use two forms of effective contraception during treatment and during the 6 months after treatment has concluded. Routine monthly pregnancy tests must be performed during this time. If pregnancy should occur during treatment or during 6 months post-therapy, the patient must be advised of the significant teratogenic risk of COPEGUS therapy to the fetus. Healthcare providers and patients are strongly encouraged to immediately report any pregnancy in a patient or partner of a patient during treatment or during 6 months after treatment cessation to the Ribavirin Pregnancy Registry at 1-800-593-2214.

Chronic hepatitis C (CHC) patients with cirrhosis may be at risk of hepatic decompensation and death when treated with alpha interferons, including PEGASYS. During treatment, patients' clinical status and hepatic function should be closely monitored, and PEGASYS treatment should be immediately discontinued if decompensation (Child-Pugh score ≥ 6) is observed. Ischemic and hemorrhagic cerebrovascular events have been observed in patients treated with interferon alfa-based therapies, including PEGASYS. Events occurred in patients with few or no reported risk factors for stroke, including patients less than 45 years of age. Because these are spontaneous reports, estimates of frequency cannot be made and causal relationship between interferon alfa-based therapies and these events is difficult to establish.

The most common adverse events reported for PEGASYS and COPEGUS combination therapy observed in clinical trials were fatigue/asthenia (65 percent), headache (43 percent), pyrexia (41 percent), myalgia (40 percent), irritability/anxiety/nervousness (33 percent), insomnia (30 percent), alopecia (28 percent), neutropenia (27 percent), nausea/vomiting (25 percent), rigors (25 percent), anorexia (24 percent), injection site reaction (23 percent), arthralgia (22 percent), depression (20 percent), pruritus (19 percent) and dermatitis (16 percent).

Serious adverse events in hepatitis C trials included neuropsychiatric disorders (homicidal ideation, suicidal ideation, suicide attempt, suicide, psychotic disorder and hallucinations), serious and severe bacterial infections (sepsis), bone marrow toxicity (cytopenia and rarely, aplastic anemia), cardiovascular disorders (hypertension, supraventricular arrhythmias and myocardial infarction), hypersensitivity (including anaphylaxis), endocrine disorders (including thyroid disorders and diabetes mellitus), autoimmune disorders (including idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura, psoriasis, lupus, rheumatoid arthritis and interstitial nephritis), pulmonary disorders (dyspnea, pneumonia, bronchiolitis obliterans, interstitial pneumonitis and sarcoidosis), colitis (ulcerative and hemorrhagic/ischemic colitis), pancreatitis, and ophthalmologic disorders (decrease or loss of vision, retinopathy including macular edema and retinal thrombosis/hemorrhages, optic neuritis and papilledema). Adverse reactions reported during post-approval use of PEGASYS therapy, with and without ribavirin, include hearing impairment, hearing loss, serious skin reactions, including erythema multiforme major, and infections (bacterial, viral and fungal).

About Roche

Hoffmann-La Roche Inc. (Roche), based in Nutley, N.J., is the U.S. pharmaceuticals headquarters of the Roche Group, one of the world's leading research-oriented healthcare groups with core businesses in pharmaceuticals and diagnostics. For more than 100 years in the U.S., Roche has been committed to developing innovative products and services that address prevention, diagnosis and treatment of diseases, thus enhancing people's health and quality of life. For additional information about the U.S. pharmaceuticals business, visit our website <http://www.rocheusa.com>. Product and treatment information for U.S. healthcare professionals is available at www.RocheExchange.com.

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- i) AIDS Epidemic Update. 2006. (Accessed October 26, 2007, at http://www.who.int/hiv/mediacentre/2006_EpiUpdate_en.pdf.)
- ii) World Health Organization. Initiative for Vaccine Research, Viral Cancers, Hepatitis C. 2006. (Accessed July 24, 2006, at http://www.who.int/vaccine_research/diseases/viral_cancers/en/index2.html%20.)

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