Pharmasset Presents R7128 14-Day Monotherapy Study Results for the Treatment of Chronic Hepatitis C; -Nucleoside polymerase inhibitor demonstrates >99% mean decrease in HCV RNA with no serious adverse events

PRINCETON, N.J., Nov. 2 /PRNewswire-FirstCall/ -- Pharmasset, Inc. (Nasdaq: VRUS) announces the results of a 14-day Phase 1 multiple ascending dose monotherapy study of R7128 for the treatment of chronic hepatitis C infection. In this study, being presented as a "late-breaker" abstract at the 58th Annual Meeting of the American Association for the Study of Liver Diseases, R7128 demonstrated potent antiviral activity and was generally safe and well-tolerated. R7128 is an orally administered prodrug of PSI-6130, a cytidine nucleoside analogue polymerase inhibitor of hepatitis C virus (HCV) that is being developed through Pharmasset's collaboration with Roche.

"R7128 has provided positive proof-of-concept that a single, direct-acting antiviral can deliver sufficient potency to suppress HCV in an interferon non-responder population," stated Dr. Michelle Berrey, Pharmasset's Vice President, Clinical Development & Chief Medical Officer. "Since robust synergy has been observed with other potent inhibitors when combined with the standard of care for HCV, we hope that these monotherapy results will translate well when R7128 is used with standard of care for longer duration in a treatment-naive population."

Dr. Rajender Reddy, Professor of Medicine and Surgery in the Division of Gastroenterology at the University of Pennsylvania and a clinical investigator in the study, noted "R7128's safety profile is encouraging, with no serious or treatment-limiting adverse events reported even at the highest dose tested. In addition, there were actually a higher number of adverse events reported in the placebo group than in the treated arms of this study. Safety is an important aspect of new HCV therapies, because the current standard of care is not always as well tolerated as desired."

The R7128 scientific presentation will be available for download in PDF format following the conference in the "R7128 Presentations & Publications" section of Pharmasset's website at http://www.pharmasset.com/pipeline/R7128-publications.asp.

R7128 Phase 1 Multiple Ascending Dose Study Overview

The Phase 1 clinical trial is a multiple center, observer-blinded, randomized and placebo-controlled study was conducted in 40 patients chronically-infected with HCV genotype 1 who previously failed interferon therapy. The primary objective was to assess the safety, tolerability and pharmacokinetics of R7128 after once-daily (QD) or twice-daily (BID) dosing for 14 days. The secondary objective was to assess antiviral activity by measuring the change in HCV RNA.

R7128 Safety Summary

R7128 was generally safe and well tolerated, and all patients completed the study. There were no serious adverse events, no adverse events requiring dose modification, no dose-related gastrointestinal adverse events and no clinically significant changes in hematologic or other laboratory parameters. The preliminary data on adverse events (AEs) reported shows the highest incidence of AEs was in the
placebo group with 34 events in 7 of 8 patients receiving placebo. During treatment in patients receiving R7128, most of the AEs reported were of mild intensity. Eighteen AEs were reported in 7 of 8 subjects that received 750mg QD, 6 AEs in 3 of 8 subjects receiving 1500mg QD, 13 AEs in 4 of 8 subjects receiving 750mg BID and 14 AEs in 4 of 8 subjects receiving 1500mg BID. The most frequently reported AEs for patients receiving R7128 were headache (13), dry mouth (3), nausea (2), fatigue (2), tiredness (2) and upper respiratory infection (2). In subjects on placebo, the most commonly reported AEs were headache (4) and diarrhea (4).

**R7128 Antiviral Activity Summary**

R7128 demonstrated potent, dose-dependent antiviral activity across the four patient cohorts (8 active, 2 placebo per cohort) receiving 750 mg or 1500 mg administered either QD or BID for 14 days as monotherapy. Both the greatest mean and maximum decrease in HCV RNA from baseline were demonstrated in the patient cohort that received 1500 mg BID. R7128 demonstrated a mean HCV RNA decrease of -0.9 log10 IU/mL (87.4%), -1.5 log10 IU/mL (96.8%), -2.1 log10 IU/mL (99.2%) and -2.7 log10 IU/mL (99.8%) in patients receiving 750mg QD, 1500mg QD, 750mg BID and 1500 mg BID, respectively. All four dose groups reached nadir values at Day 15. A maximum -4.2 log10 IU/mL (99.9%) HCV RNA decrease was demonstrated in a patient following 14 days of monotherapy with 1500 mg BID of R7128, which was also below the level of detection (<15 IU/ml). There was no clinical evidence of viral rebound in any dose cohort during the 14 days of dosing, which provides early evidence of high genetic barrier for nucleoside inhibitors of NS5b polymerase.

Pharmasset is currently enrolling a 4-week Phase 1 clinical trial to evaluate R7128 in combination with Pegasys(R) (pegylated interferon) plus Copegus(R) (ribavirin) in up to 75 treatment-naïve patients chronically infected with hepatitis C virus (HCV) genotype 1. The primary objective is to assess the safety, tolerability and pharmacokinetics of R7128 in combination with Pegasys plus Copegus. The secondary objective is to evaluate the short-term change in HCV RNA. The study will investigate up to three oral dose levels of R7128 (500 mg to 1500 mg) administered twice-daily with Pegasys plus Copegus for 4 weeks. Please see [www.clinicaltrials.gov](http://www.clinicaltrials.gov) or e-mail clinicaltrials@pharmasset.com for more information.

**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 B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV).

Pharmasset is currently developing three product candidates. Clevudine, for the treatment of chronic HBV infection, is enrolling Phase 3 clinical trials for registration in the Americas and Europe. Clevudine is already approved for HBV in South Korea and marketed by Bukwang Pharmaceuticals in South Korea under the brand name Leovirid. R7128, an orally administered treatment for chronic HCV infection, is enrolling a 4-week Phase 1 clinical trial in combination with Pegasys(R) and Copegus(R) through a strategic collaboration with Roche. Racivir, which is being developed for the treatment of HIV in combination with other approved HIV drugs, has completed a Phase 2 clinical trial.
About R7128

R7128 is being developed for the treatment of chronic HCV infection. R7128 is a prodrug of PSI-6130, a pyrimidine nucleoside analog inhibitor of HCV RNA polymerase. A prodrug is a chemically modified form of a molecule designed to enhance the absorption, distribution and metabolic properties of that molecule. Results from an oral single ascending dose study of PSI-6130 in 24 healthy male volunteers showed that PSI-6130 was generally well tolerated with no serious adverse events in doses up to 3000 mg.

About Hepatitis C

Hepatitis C is a blood-borne infectious disease of the liver and is a leading cause of chronic liver disease and liver transplants. The WHO estimates that nearly 180 million people worldwide, or approximately 3% of the world's population, are infected with hepatitis C virus (HCV). The CDC has reported that almost four million people in the United States have been infected with HCV, of whom 2.7 million are chronically infected.

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