



## Pharmasset Initiates Phase 1b Multiple Ascending Dose Clinical Trial of PSI-938 in Patients with Chronic Hepatitis C

- PSI-938 single ascending dose study in healthy volunteers supports progression to 7 day monotherapy study in HCV infected patients
- PSI-938 was generally safe and well tolerated with no dose-limiting toxicity
- Further results from single ascending and multiple ascending dose trials are expected in the third quarter 2010

**PRINCETON, NJ - (July 28, 2010)** - Pharmasset, Inc. (Nasdaq: VRUS) announced today that safety and pharmacokinetic data from the PSI-352938 ("PSI-938") single ascending dose study support progression to a multiple ascending dose trial with PSI-938, which has initiated dosing. PSI-938 is a guanine nucleotide analog polymerase inhibitor for the treatment of chronic hepatitis C virus (HCV) infection. This study is designed to assess the safety, tolerability and antiviral activity of PSI-938 monotherapy administered over 7 days in HCV-infected individuals.

"PSI-938 is the third differentiated nucleoside analog that Pharmasset has advanced into clinical development for HCV," stated Michelle Berrey, MD, MPH, Pharmasset's Chief Medical Officer. "As with RG7128 and PSI-7977, PSI-938 demonstrates a high barrier to resistance in vitro; but unlike the cytidine and uridine analogs, PSI-938 retains equivalent potency against the S282T mutant. As the HCV field moves toward IFN-sparing, all-oral DAA combinations, we continue to believe nucleosides could become the backbone of care given these differentiating attributes and have the potential to be combined with all DAA classes."

### PSI-938 Phase 1 Program Overview

The Phase 1 program is investigating the safety, tolerability and pharmacokinetics of PSI-938 in healthy subjects following escalating single doses (Phase 1a), and in patients chronically infected with HCV genotype 1 following repeat dosing for 7 days (Phase 1b). The Phase 1b study will additionally investigate hepatitis C viral dynamics and monitor for the development of drug resistance.

Subjects in the Phase 1a single ascending dose study received single doses of PSI-938 ranging from 100 mg to 800 mg or a matching placebo. Preliminary data from the phase 1a single ascending dose study includes:

- No serious adverse events or discontinuations;
- No dose-related adverse events or dose-limiting toxicity;
- No grade III / IV lab abnormalities;
- No clinically significant changes in vital signs or ECGs; and
- PK which supports QD dosing.

A Phase 1b multiple ascending dose trial has now been initiated in treatment-naïve patients with chronic HCV genotype 1 infection. Subjects will be enrolled at multiple centers in the US and randomized to PSI-938 or placebo. Based upon the results from the first time in human study, the first dose of PSI-938 to be tested will be 100 mg administered once daily. The primary objectives of this study are to assess the safety, tolerability, pharmacokinetics and viral dynamics of PSI-938 after repeat dosing over 7 days.

Results from both studies are expected in the third quarter of 2010.

### Purine and Pyrimidine Analogs

Pharmasset's purine nucleoside/tide analogs share many of the benefits of pyrimidine nucleoside/tide analogs, such as RG7128 and PSI-7977, in that they have demonstrated in vitro activity across multiple HCV genotypes, have a higher barrier to resistance than other classes of HCV small molecules in development, and, in spite of the prodrug technology, have no CYP 3A4 liability and thus a lower risk of drug interactions when combined with other direct acting antivirals targeting HCV. In addition, Pharmasset's purine analogs retain equivalent potency against wild type HCV and virus with the S282T mutation associated with in vitro resistance in other nucleoside/tide analogs in development. Furthermore, the purines are metabolized to the active triphosphate form through a different phosphorylation pathway than the pyrimidine analogs, thus decreasing the risk of competition between the two analogs for conversion to the active triphosphate. Given these characteristics, Pharmasset's purine and pyrimidine analogs have the potential to be combined as part of a future treatment regimen, which will be the focus

of upcoming trials.

### **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, secondarily, on the development of Racivir™ for the treatment of human immunodeficiency virus (HIV). Our research and development efforts focus on nucleoside/tide analogs, a class of compounds which act as alternative substrates for the viral polymerase, thus inhibiting viral replication. We currently have four clinical-stage product candidates. RG7128, a cytosine analog for chronic HCV infection, is in two Phase 2b clinical studies in combination with Pegasys® plus Copegus® and is also in the INFORM studies, the first series of studies designed to assess the potential of combinations of small molecules without Pegasys® and Copegus® to treat chronic HCV. These clinical studies are being conducted through a strategic collaboration with Roche. Our other clinical stage HCV candidates include PSI-7977, an unpartnered uracil nucleotide analog that has recently completed a Phase 2a study, and PSI-938, an unpartnered guanine nucleotide analog in Phase 1. We also have in our pipeline an additional purine nucleotide analog, PSI-661, in advanced preclinical development. Racivir, for the treatment of HIV, has completed a Phase 2 clinical study.

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### **Forward-Looking Statements**

*Pharmasset "Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995: Statements in this press release that are not historical facts are "forward-looking statements," including, without limitation, statements that involve risks, uncertainties, and other important factors, including, without limitation, the risk of 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 risks, uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended September 30, 2009 and our Quarterly Reports on Form 10-Q for the periods ended December 31, 2009 and March 31, 2010 filed with the Securities and Exchange Commission and discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission.*