



October 25, 2010

## **Vertex Pharmaceuticals Announces Start of a Phase 3b Study of Twice-Daily Telaprevir in People Not Treated Previously for Hepatitis C**

**- First Phase 3 study to evaluate twice-daily (BID) dosing of a protease inhibitor for hepatitis C -  
- All patients will receive telaprevir-based combination therapy -**

CAMBRIDGE, Mass., Oct 25, 2010 (BUSINESS WIRE) -- Vertex Pharmaceuticals Incorporated (Nasdaq: VRTX) today announced the initiation of a Phase 3b study called OPTIMIZE that will evaluate twice-daily (BID) dosing of a telaprevir-based combination regimen in people chronically infected with genotype 1 hepatitis C virus (HCV) who have not been treated previously. This is the first Phase 3 study to evaluate twice-daily dosing of a protease inhibitor for the treatment of hepatitis C. OPTIMIZE will not include a control arm of pegylated-interferon and ribavirin alone.

"The sustained viral response rates, or viral cures, seen across a broad range of people in the Phase 3 studies of telaprevir set a high bar in the development of treatments for hepatitis C, and we are committed to studying new ways to further improve treatment," said Robert Kauffman, M.D., Ph.D., Senior Vice President and Chief Medical Officer for Vertex. "High viral cure rates were demonstrated in the Phase 2 study of twice-daily telaprevir and we're looking forward to conducting a larger study to confirm these findings."

The OPTIMIZE study will be conducted by Vertex's collaborator, Tibotec.

### **OPTIMIZE Study Design**

In Vertex's recently completed Phase 3 registration program, patients who received telaprevir in combination with pegylated-interferon and ribavirin took telaprevir three times daily (750mg; every eight hours). OPTIMIZE is a randomized, open-label, Phase 3b study that will evaluate twice-daily dosing (BID) of telaprevir in people chronically infected with genotype 1 HCV who have not been treated previously. The study will be conducted globally at 135 clinical trial sites and enroll approximately 700 people. Patient screening for enrollment in the OPTIMIZE study is expected to start in November 2010.

For the first 12 weeks of the study, all patients will receive 2,250mg of telaprevir taken twice daily (1,125mg; BID) or three times daily (750mg; every eight hours) in combination with pegylated-interferon alpha-2a (PEGASYS<sup>(R)</sup>) and twice-daily ribavirin. Response guided therapy will be used to determine whether patients receive pegylated-interferon and ribavirin alone for an additional 12 weeks (24 weeks total) or 36 weeks (48 weeks total) based on their treatment response at week 4. The primary endpoint of the OPTIMIZE study is sustained viral response (SVR) 24 weeks after the end of all treatment. The primary objective is to demonstrate non-inferiority of BID telaprevir versus telaprevir dosed every eight hours as measured by SVR.

SVR data from the study are expected as early as 2012. If these data are positive, they may support the submission of a supplemental New Drug Application (sNDA) for twice-daily (BID) dosing of telaprevir.

### **Phase 2 C208 study**

Study C208 was an exploratory, four-arm, randomized, open label, Phase 2 clinical trial that was conducted by Tibotec in Europe in 161 treatment-naïve patients with genotype 1 HCV infection. The objective of Study C208 was to explore the safety, efficacy, tolerability and pharmacokinetics of telaprevir administered every 12 hours (1,125mg) or every eight hours (750mg). Each dosing regimen of telaprevir was studied in combination with either PEGASYS<sup>(R)</sup> or PEGINTRON<sup>(R)</sup> and ribavirin, the currently approved therapies for chronic HCV infection.

Across the four arms, SVR rates were 82% and 83% in patients treated with telaprevir-based regimens every 12 hours (PEGINTRON and PEGASYS, respectively) and 81% and 85% in patients treated with the every 8-hour regimen (PEGINTRON and PEGASYS, respectively). The primary endpoint was SVR, and data from this study were presented at the 2009 annual meeting of the American Association for the Study of Liver Diseases (AASLD). The Phase 2 C208 data supported the initiation of the Phase 3b OPTIMIZE study.

In the C208 study, the frequency and severity of adverse events (AEs) and the rate of treatment discontinuations were similar

to those reported in prior telaprevir trials. The rates of viral breakthrough were similar to the every 8- and every 12-hour regimens. The most common adverse events reported in patients in Study C208 were pruritis, nausea, rash, anemia, flu-like illness, fatigue and headache, and were similar overall between the patient groups receiving every 8-hour dosing and those receiving every 12-hour dosing.

Updates on the status of clinical trials of telaprevir are available online at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

## **About the Telaprevir Development Program**

To date, more than 2,500 people with hepatitis C have received telaprevir-based therapy as part of Phase 2 studies and the Phase 3 ADVANCE, ILLUMINATE and REALIZE studies. Together, these studies enrolled people with genotype 1 hepatitis C who had not been treated for their disease previously (ADVANCE and ILLUMINATE) as well as people who had been treated before but did not achieve a viral cure (REALIZE). A fact sheet on the Phase 3 Telaprevir Development Program is available at <http://www.vrtx.com/aasld2010.html>.

### *Phase 3 ADVANCE Trial*

The pivotal Phase 3 ADVANCE study evaluated telaprevir-based response-guided regimens in 1,095 treatment-naïve patients. The primary endpoint of ADVANCE was SVR, defined as the proportion of people who had undetectable HCV RNA both at the end of treatment and 24 weeks after the end of treatment. The secondary endpoint was to evaluate the safety of telaprevir when dosed in combination with pegylated-interferon and ribavirin. As part of a response-guided design, people in the telaprevir-based treatment arms who had undetectable HCV RNA (<25IU/mL, and undetectable by Roche COBAS Taqman HCV test) at weeks 4 and 12 of treatment were eligible to receive a total of 24 weeks of therapy. Patients who did not meet the response-guided criterion but were undetectable at week 24, received 48 weeks of total therapy.

### *Phase 3 ILLUMINATE Trial*

The ILLUMINATE trial was a supplemental, open-label, Phase 3 study designed to evaluate whether there was any benefit in extending therapy from 24 to 48 weeks in people whose hepatitis C was undetectable (<25IU/mL undetectable) at weeks 4 and 12 of therapy. The primary endpoint of the study was the proportion of people who achieved SVR in the randomized treatment groups, and evaluated by a non-inferiority analysis.

### *Phase 3 REALIZE Trial*

REALIZE was the second Phase 3 pivotal trial designed to evaluate telaprevir-based regimens in people who had received pegylated-interferon based therapy but did not achieve a cure. REALIZE was the only Phase 3 clinical trial to date of an investigational direct-acting antiviral (DAA) to include all major subgroups of difficult-to-treat patients including null responders, defined as people who had a less than 2 log<sub>10</sub> reduction in viral load by week 12 of a prior course of therapy.

Vertex retains commercial rights to telaprevir in North America. Tibotec has rights to commercialize telaprevir in Europe, South America, Australia, the Middle East and certain other countries. Mitsubishi Tanabe Pharma has rights to commercialize telaprevir in Japan and certain Far East countries.

## **About Hepatitis C**

Hepatitis C is a liver disease caused by the hepatitis C virus, which is found in the blood of people with the disease.<sup>2</sup> According to a 2010 report from the Institute of Medicine, up to 3.9 million people in the United States have chronic hepatitis C and 75% of those infected are unaware of their infection.<sup>3</sup> Approximately 60 percent of genotype 1 patients who undergo an initial 48-week regimen with pegylated-interferon and ribavirin, the currently approved treatment regimen, do not achieve SVR,<sup>4,5,6</sup> or viral cure.<sup>1</sup>

Hepatitis C is spread through direct contact with the blood of infected people.<sup>2</sup> Though many people with hepatitis C may not experience symptoms, others may have symptoms such as fatigue, fever, jaundice and abdominal pain.<sup>2</sup> Chronic hepatitis C can lead to serious and life-threatening liver problems, including liver damage, cirrhosis, liver failure or liver cancer.<sup>2</sup> If treatment is not successful and a person does not achieve a viral cure, they remain at an increased risk for progressive liver disease.<sup>7,8,9,10,11</sup> In the United States, hepatitis C is the leading cause of liver transplantations and is reported to contribute to 4,600 to 12,000 deaths annually.<sup>8</sup> The majority of people with hepatitis C were born between 1946 and 1964, accounting for two of every three people with chronic hepatitis C.<sup>11</sup> By 2029, total annual medical costs in the U.S. for people with hepatitis C are expected to more than double, from \$30 billion in 2009 to approximately \$85 billion.<sup>11</sup>

Additional resources for media, including a hepatitis C backgrounder and glossary of common terms, are available at: <http://investors.vrtx.com/press.cfm>

## 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 companies. Vertex's product pipeline is focused on viral diseases, cystic fibrosis, inflammation, autoimmune diseases, epilepsy, cancer and pain.

Vertex co-discovered the HIV protease inhibitor, Lexiva, with GlaxoSmithKline.

Lexiva is a registered trademark of the GlaxoSmithKline group of companies.

PEGASYS<sup>(R)</sup> and COPEGASYS<sup>(R)</sup> are registered trademarks of Hoffman-La Roche.

## References:

- <sup>1</sup> Ghany, m.G., Strader, d.B., Thomas, d.L., Seeff, Leonard B. Diagnosis, Management and Treatment of Hepatitis C; An Update. 2009. *Hepatology*. 2009;49 (4):1-40.
- <sup>2</sup> Centers for Disease Control and Prevention. Hepatitis C Fact Sheet: CDC Viral Hepatitis. Available at: <http://www.cdc.gov/hepatitis/HCV/PDFs/HepCGeneralFactSheet.pdf>. Accessed May 25, 2010.
- <sup>3</sup> Institute of Medicine. Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C. Available at <http://www.iom.edu/Reports/2010/Hepatitis-and-Liver-Cancer-A-National-Strategy-for-Prevention-and-Control-of-Hepatitis-B-and-C.aspx>. Accessed May 25, 2010.
- <sup>4</sup> Manns MP, McHutchison JG, Gordon SC, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. *Lancet*. 2001;358:958-965.
- <sup>5</sup> Fried MW, Shiffman ML, Reddy KR, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *N Engl J Med*. 2002;347:975-982.
- <sup>6</sup> McHutchison JG, Lawitz EJ, Shiffman ML, et al; IDEAL Study Team. Peginterferon alfa-2b or alfa-2a with ribavirin for treatment of hepatitis C infection. *N Engl J Med*. 2009;361:580-593.
- <sup>7</sup> Morgan T.R, Ghany MG, Kim HY, Snow KK, Lindsay K, Lok AS. Outcome of sustained virological responders and non-responders in the Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis (HALT-C) trial. *Hepatology*. 2008;50(Suppl 4):357A (Abstract 115).
- <sup>8</sup> Davis GL, Alter MJ, El-Serag H, Poynard T, Jennings LW. Aging of hepatitis C virus (HCV)-infected persons in the United States: A multiple cohort model of HCV prevalence and disease progression. *Gastroenterology*. 2010;138: 513-521
- <sup>9</sup> Volk, Michael I., Tocco, Rachel, Saini, Sameer, Lok, Anna S.F. Public Health Impact of Antiviral Therapy for Hepatitis C in the United States. *Hepatology*.2009;50(6):1750-1755.
- <sup>10</sup> Veldt, B.J., Heathcote, J., Wedmeyer, H. Sustained virologic response and clinical outcomes in patients with chronic hepatitis C and advanced fibrosis. *Annals of Internal Medicine*. 2007; 147: 677-684.
- <sup>11</sup> Pyenson, B., Fitch, K., Iwasaki, K. Consequences of Hepatitis C Virus (HCV): Costs of a Baby Boomer Epidemic of Liver Disease. Milliman, Inc. This report was commissioned by Vertex Pharmaceuticals, Inc. May, 2009.

## Safe Harbor Statement

This press release contains forward-looking statements, including statements regarding (i) the viral cure rates in Phase 3 studies of telaprevir setting a high bar in the development of treatments for HCV and the Company's commitment to studying new ways to further improve treatment; (ii) the possibility that a larger study will confirm the findings from the Phase 2 study of twice-daily telaprevir; (iii) the design of the trial, including the objective of the trial and the primary endpoint, the expectation that patient screening will start in November 2010, the number of patients the Company expects to enroll, and the number and location of clinical trial sites, and that the trial will be conducted by Tibotec; (iv) the expectation that SVR data from the trial will be available as early as 2012 and (v) the expectation that if the data are positive they may support the submission of a supplemental New Drug Application for twice-daily dosing of telaprevir. While the company believes the forward-looking statements contained in this press release are accurate, those statements are subject to risks and uncertainties that could cause actual outcomes to vary materially from the outcomes referenced in the forward-looking statements. These risks and uncertainties include, among other things, the risk that efforts to develop telaprevir may not proceed due to technical, scientific, commercial, financial or other reasons, that clinical trials may not proceed as planned due to drug supply or patient enrollment issues, that additional clinical trials of telaprevir dosed twice-daily may not reflect the results obtained to date, that an adverse event profile for telaprevir could be revealed in further nonclinical or clinical studies that could put further development of telaprevir in jeopardy or adversely impact their therapeutic value and other risks listed under Risk Factors in Vertex's annual

report and quarterly reports filed with the Securities and Exchange Commission and available through the Company's website at [www.vrtx.com](http://www.vrtx.com). Vertex disclaims any obligation to update the information contained in this press release as new information becomes available.

(VRTX-GEN)

SOURCE: Vertex Pharmaceuticals Incorporated

Vertex Pharmaceuticals Incorporated

**Media:**

Amy Pasqua, 617-444-6992

or

Dawn Kalmar, 617-444-6992

or

Zachry Barber, 617-444-6992

or

**Investors:**

Michael Partridge, 617-444-6108

or

Lora Pike, 617-444-6755

or

Matthew Osborne, 617-444-6057

Copyright Business Wire 2010