



## **Tibotec to present final safety and efficacy results from phase 2b PILLAR study of Once-daily TMC435 in late-breaker at AASLD**

### **Data show high rates of virologic response and shortened treatment duration; safety and tolerability comparable to placebo**

**San Francisco, CA, November 5th, 2011** – Tibotec Pharmaceuticals (Tibotec), one of the Janssen (Janssen) Pharmaceutical Companies, today will present results of the final analysis of PILLAR, a phase 2b study of the investigational hepatitis C virus (HCV) NS3/4A protease inhibitor TMC435 in treatment-naïve patients with chronic genotype 1 HCV, as part of a late-breaker oral presentation at the 62nd Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) in San Francisco, CA, USA.

Results from the final PILLAR analysis showed that TMC435 administered in combination with peginterferon  $\alpha$ -2a and ribavirin (PR) resulted in significantly higher sustained virologic response (SVR) rates compared to placebo plus PR. In the two TMC435 treatment groups administered TMC435 75mg, 75 and 82 percent of patients achieved SVR24, and in the two TMC435 treatment groups administered TMC435 150mg, 81 and 86 percent of patients achieved SVR24, compared to 65 percent of patients treated in the placebo arm. In addition, 79 to 86 percent of patients in the TMC435 treatment arms had a shortened treatment duration of 24 weeks, compared to a 48 weeks treatment duration for patients who received placebo plus P/R. In TMC435 arms, 68 to 76 percent of patients achieved rapid virologic response [RVR; HCV RNA<25 (undetectable)], of whom 88 to 95 percent achieved SVR24. There were no significant differences for adverse events between TMC435 treatment groups and placebo. TMC435 150mg administered once daily (q.d.) is being investigated in phase 3 trials in treatment-naïve patients and in patients who experienced a viral relapse after being treated with interferon-based therapy. TMC435 is being developed by Tibotec Pharmaceuticals. Medivir AB has commercialization rights for TMC435 for the Nordic countries, Janssen has commercialization rights for TMC435 in the rest of the world.

The PILLAR study [Protease Inhibitor TMC435 trial assessing the optimal dose and duration as once daily Anti-viral Regimen] (TMC435-C205; NCT00882908) was a five-arm, global phase 2b randomized, double-blind, placebo controlled study in 386 treatment-naïve patients. TMC435 was administered in doses of 75mg or 150mg q.d. for either 12 weeks or 24 weeks in combination with 24 or 48 weeks of peg-interferon and ribavirin (PR). Patients in the placebo arm receive 24 weeks of placebo plus peg-interferon and ribavirin followed by 24 additional weeks of peg-interferon and ribavirin treatment. The primary endpoint of the study was sustained virologic response at Week-72 (SVR week 72). The PILLAR study was conducted in 13 countries in Europe, North America, and Australasia.

Patients receiving TMC435 were allowed to stop all treatment at week 24 if they met both response-guided criteria: a) detectable or undetectable HCV RNA levels (< 25 IU/mL) at week 4 and b) undetectable HCV RNA at weeks 12, 16 and 20. Patients who did not meet the above response-guided criteria continued with peg-interferon and ribavirin until Week-48.

"HCV is a devastating problem worldwide and remains a leading cause of cirrhosis, liver cancer, and liver transplantation worldwide," said Dr Michael W. Fried M.D., lead clinical investigator and Professor of Medicine, Director of Hepatology, University of North Carolina at Chapel Hill. "We are extremely encouraged and excited by the success of once-daily TMC435 in achieving statistically significant higher SVR compared to control group and look forward to furthering its development in recently launched phase 3 trials."

The goal of HCV treatment is to achieve SVR24, which means the virus is undetectable in patients' blood six months after they have finished treatment. Patients who achieve SVR are considered cured.

The most common adverse events (AEs) in the PILLAR study were headache and fatigue, 46 percent and 42 percent in the TMC435 groups and 51 percent and 47 percent in the placebo group respectively. There were no clinically significant differences in frequency of rash, anemia or gastrointestinal events between the TMC435 groups and placebo. Most AEs were mild to moderate in severity. AEs leading to treatment discontinuation of TMC435/placebo were reported in 7.1 percent of patients in TMC435 arms and 7.8 percent in placebo arm.

"Tibotec is pleased to present the final results of the phase 2b PILLAR study at AASLD. The continued development of TMC435, which is currently being investigated in registrational phase 3 studies, reinforces our strong commitment to the development of new therapies that may reduce treatment duration and improve the lives of those impacted by HCV," said Maria Beumont M.D., Global Medical Leader TMC435 at Tibotec.

In conjunction with the final sustained virologic response (SVR) results from PILLAR, Tibotec is presenting virology analysis data from PILLAR and two sets of early study results on the effects of co-administering TMC435 and methadone and its

interaction with the antidepressant escitalopram, to be featured in 3 posters at AASLD:

- "TMC435 in combination with peginterferon alpha-2a/ribavirin in treatment-naïve patients infected with HCV genotype 1: virology analysis of the PILLAR study." O. Lenz.
- "The pharmacokinetic interaction between the investigational NS3-4A HCV protease inhibitor TMC435 and methadone." M. Beumont-Mauviel.
- "The pharmacokinetic interaction between the investigational HCV NS3/4A protease inhibitor TMC435 and escitalopram." M. Beumont-Mauviel.

Tibotec is currently conducting two global, phase 3 registrational trials to examine TMC435 in treatment-naïve adults with chronic genotype 1 hepatitis C virus (HCV). A third global phase 3 trial is being conducted in genotype 1 HCV patients who have experienced a viral relapse after prior interferon-based treatment. All three studies are fully randomized.

### **About HCV**

HCV is a blood-borne infectious disease that affects the liver.<sup>1</sup> With an estimated 170 million people infected worldwide<sup>1</sup> and three to four million people newly infected each year,<sup>2</sup> HCV puts a significant burden on patients and society. Chronic infection with HCV can lead to liver cancer and other serious and fatal liver diseases, and is the most common cause of liver transplant worldwide.<sup>3</sup> Pegylated interferon combined with ribavirin causes serious side effects and only cures 40 to 50 percent of genotype 1 patients. The development of new therapies, particularly direct antivirals with different modes of action, may allow HCV patients to undergo a shorter and more effective treatment regimen.<sup>4,5,6,7</sup>

### **About Tibotec Pharmaceuticals**

Tibotec Pharmaceuticals, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, is a global pharmaceutical and research development company. The Company's main research and development facilities are in Beerse, Belgium with offices in Titusville, NJ and Cork, Ireland. Tibotec is dedicated to the discovery and development of innovative HIV/AIDS and hepatitis C drugs, and anti-infectives for diseases of high unmet medical need.

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3 Roche B, Samuel D., Villejuif, France. Risk factors for hepatitis C recurrence after liver transplantation. Journal of Viral Hepatitis. 2007 Nov;14. Suppl 1:89-96.

4 Manns P, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. The Lancet. 2001 Sep 22; 358 (9286):958-65.

5 Fried M, et al. Peginterferon Alfa-2a plus Ribavirin for Chronic Hepatitis C Virus Infection. New England Journal of Medicine 2002; 347:975-982.

6 Hadziyannis S, et al. Peginterferon- $\alpha$ 2a and Ribavirin Combination Therapy in Chronic Hepatitis C: A Randomized Study of Treatment Duration and Ribavirin Dose. Annals of Internal Medicine 2004 March; 140 (5):346-355.

7 Hutchison, J et al. Peginterferon Alfa-2b or Alfa-2a with Ribavirin for Treatment of Hepatitis C Infection. New England Journal of Medicine 2009; 361:580-593.

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