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## **INCIVO<sup>®</sup> Receives Positive Opinion From The Committee For Medicinal Products For Human Use (CHMP) For Twice Daily Dosing For Treatment Of Genotype-1 Hepatitis C Virus**

**OPTIMIZE study results presented at EASL show similar sustained virological response (SVR12) rates in patients with fibrosis or cirrhosis receiving an INCIVO<sup>®</sup> (telaprevir) combination treatment twice daily versus every eight hours**

**Beerse, Belgium, 26 April, 2013** - Janssen Infectious Diseases-Diagnostics BVBA (Janssen), announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending the approval of twice daily (BID) dosing of INCIVO<sup>®</sup> (telaprevir), a direct acting antiviral (DAA) for the treatment of chronic genotype-1 hepatitis C virus (HCV), in combination with pegylated-interferon and ribavirin (PR).

The CHMP positive opinion is a critical step in the approval process and will be considered by the European Commission, which has authority to approve medicines for use throughout the European Union. The current approved dose for INCIVO is 750 mg every 8 hours in combination with PR.

"This positive opinion from the CHMP is an important development for a more convenient treatment regimen for patients which should help lead to greater adherence, a critical factor in HCV treatment," said Gaston Picchio, Hepatitis Disease Area Leader at Janssen R&D. "Telaprevir has already played a huge part in improving treatment outcomes for people living with hepatitis C with more than 80,000 people treated to date globally with telaprevir combination treatment. This recommendation is the next step in our commitment to improving the lives of more people living with hepatitis C and supporting healthcare professionals around the world."

Janssen presented clinical trial results showing that the relative efficacy of a twice daily (BID) investigational dosing regimen of INCIVO<sup>®</sup> (telaprevir) 1125 mg combination treatment was similar to an every eight hours (q8h) regimen of INCIVO<sup>®</sup> (telaprevir) 750 mg combination treatment in HCV genotype-1 patients regardless of fibrosis or cirrhosis based on sustained virological response rates at 12 weeks after the last treatment dose (SVR12).<sup>1</sup> These results, a sub-analysis from the OPTIMIZE Phase 3 trial, were presented during the 48<sup>th</sup> annual meeting of the European Association for the Study of the Liver (EASL) in Amsterdam (<http://www.easl.eu/the-international-liver-congress>). Additional sub-analyses from this study evaluating anemia management,<sup>2</sup> efficacy in patients by the IL28B genotype<sup>3</sup> and patient adherence<sup>4</sup> were also presented.

"Simplifying available treatment regimens for HCV, without compromising on cure rates is especially important for patients with fibrosis or cirrhosis. We know that telaprevir combination treatment offers patients improved cure rates over treatment with pegylated interferon and ribavirin alone. These results confirm that a twice daily dosing schedule for a telaprevir-based regimen gives patients a similar chance of achieving SVR12 as the current approved dose in a population who desperately need more effective treatment," said Yves Horsmans, Lead Study Investigator and Professor at Cliniques Universitaires Saint-Luc, Belgium.

Results from the sub-analysis of the 740 patients included in the OPTIMIZE study showed that those with cirrhosis who received a twice daily dose of telaprevir 1125 mg in combination with PR, achieved similar SVR12 rates compared with those who received telaprevir 750 mg every 8 hours in combination with PR (54% versus 49%).<sup>1</sup> Patients at other stages of fibrosis, F0 to F4, also achieved similar SVR12 rates with a twice daily dose of telaprevir 1125 mg in combination with PR compared with those who received telaprevir 750 mg every 8 hours in combination with PR (see table 1).

**Table 1: SVR 12 rates, HCV RNA<25 IU/mL, 12 weeks after last planned dose of PR**

|   | Fibrosis         |                 | Cirrhosis<br>n=103 | w/o Cirrhosis<br>n=636 |
|---|------------------|-----------------|--------------------|------------------------|
|   | F0-2<br>n=529    | F3-4<br>n=210   |                    |                        |
| Telaprevir dosing                       |                  |                 |                    |                        |
| Telaprevir 1125 mg<br>twice daily + PR  | 80%<br>(213/267) | 60%<br>(61/102) | 54%<br>(29/54)     | 78%<br>(245/315)       |
| Telaprevir 750 mg<br>every 8 hours + PR | 79%<br>(208/262) | 57%<br>(62/108) | 49%<br>(24/49)     | 77%<br>(246/321)       |

The safety and tolerability of telaprevir across fibrosis or cirrhosis stages were consistent with previous studies.<sup>1</sup> Grade 3 or 4 adverse events (AEs) were reported in 41% of patients with and 40% of patients without cirrhosis.<sup>1</sup> Serious adverse events and discontinuations due to adverse events were higher in patients with cirrhosis than those without (14% and 21% vs 8% and 16%, respectively).<sup>1</sup> The most common adverse events experienced were fatigue, pruritus, anemia, nausea and rash.<sup>5</sup> The proportion of patients who experienced a low haemoglobin level ( $\leq 10\text{g/dL}$ ) was higher among patients with (50%) than without cirrhosis (42%).<sup>1</sup>

Results from an additional sub-analysis of the OPTIMIZE study found that adherence was greater in patients who received twice daily dosing of telaprevir compared to every eight hours.<sup>4</sup> "Treating HCV can be complex and therefore anything that can help make effective treatments simpler and adherence easier for patients will ultimately improve their chance of achieving a cure," said study investigator Dr Maria Buti, Hospital Val d'Hebron, Spain.

**Additional telaprevir data from the OPTIMIZE study presented at EASL includes\*:**

- Anemia and its management in patients treated with telaprevir twice daily<sup>2</sup>
- Efficacy of telaprevir dosed twice daily versus every 8 hours by IL28B genotype<sup>3</sup>
- Adherence with telaprevir BID vs q8h dosing in treatment-naïve HCV-infected patients<sup>4</sup>

**\*Poster session: Friday, April 26 from 9:030 AM-6:00 PM**

**Additional telaprevir data presented at EASL includes\*:**

- Management and outcomes of anemia in the International Telaprevir Early Access Program, for patients with hepatitis C genotype 1 infection<sup>6</sup>
- Treatment with telaprevir-based therapy after exposure to peg-IFN/RBV in the REALIZE study<sup>7</sup>
- Treatment with telaprevir/peg-IFN/RBV after 14-day telaprevir exposure in Phase I studies<sup>8</sup>
- High SVR rates (SVR4) for 12?week total telaprevir combination therapy in IL28B CC treatment-naïves and prior relapsers with G1 chronic hepatitis C: CONCISE interim analysis<sup>9</sup>

**\*Poster session: Friday, April 26 from 9:00 AM-6:00 PM**

**About OPTIMIZE**

OPTIMIZE is a randomized, open-label, multicenter Phase 3 study in patients with genotype-1 chronic HCV infection who have not been previously treated. During the study, 740 patients were randomized to receive either a twice daily (BID) dosing of INCIVO<sup>®</sup> (telaprevir) 1125 mg or dosing every 8 hours (q8h) of INCIVO<sup>®</sup> (telaprevir) 750 mg, each in combination with PR. At 12 weeks, telaprevir treatment ended and patients continued on PR alone for up to week 24 or week 48 depending on their viral response at week 4. Patients were followed up for a further 12 weeks to monitor SVR rates (SVR12).<sup>5</sup>

**About INCIVO<sup>®</sup> (telaprevir)**

INCIVO<sup>®</sup> (telaprevir), in combination with peginterferon alfa and ribavirin (PR), is indicated for the treatment of genotype-1 chronic HCV in adult patients with compensated liver disease (including cirrhosis) who are treatment-naïve, and who have previously been treated with interferon alfa (pegylated or non pegylated) alone or in combination with ribavirin, including

relapsers, partial responders and null responders.<sup>10</sup> INCIVO<sup>®</sup> is a small molecule, selective inhibitor of the HCV serine protease, and a member of the new class of medicine for the treatment of genotype-1 chronic HCV, direct acting antivirals (DAAs). Unlike previous treatments, DAAs act directly on viral enzymes and prevent the virus from replicating. INCIVO<sup>®</sup> was approved by the European Commission on the 19<sup>th</sup> September 2011. The current approved dose for INCIVO<sup>®</sup> is 750 mg every 8 hours in combination with PR.

INCIVO<sup>®</sup> was developed by Janssen Infectious Diseases-Diagnostics BVBA, one of the Janssen Pharmaceutical Companies, in collaboration with Vertex Pharmaceuticals Incorporated (Vertex) and Mitsubishi Tanabe Pharma Corporation (Mitsubishi Tanabe Pharma). Janssen has rights to commercialize telaprevir in Europe, South America, Australia, the Middle East and certain other countries. Vertex has rights to commercialize telaprevir in North America where it is being marketed under the brand name INCIVEK<sup>™</sup>. Mitsubishi Tanabe Pharma has rights to commercialize telaprevir in Japan and certain Far East countries where it is being marketed as TELAVIC<sup>®</sup>.

### **Important Safety Information**

Please see full Summary of Product Characteristics or visit <http://www.emea.europa.eu> for more details.

The overall safety profile of telaprevir is based on the Phase II/III clinical development programme containing 2,641 patients who received a telaprevir based regimen. In clinical trials, the incidence of adverse events of at least moderate intensity was higher in the telaprevir group than in the placebo group (both groups receiving peginterferon alfa and ribavirin). The most frequently reported adverse reactions (incidence  $\geq$  5.0%) of at least grade 2 in severity were anemia, rash, pruritus, nausea, and diarrhoea during the telaprevir treatment phase, and the most frequently reported adverse reactions (incidence  $\geq$  1.0%) of at least Grade 3 were anemia, rash, thrombocytopenia, lymphopenia, pruritus, and nausea. INCIVO<sup>®</sup> prescribing information includes special warnings and pre-cautions for use with regards to severe rash including Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) and Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN).<sup>10</sup>

Rash events were reported in 55% of patients with a telaprevir based regimen compared to 33% of patients treated with peginterferon alfa and ribavirin only and more than 90% of rashes were of mild or moderate severity. Severe rashes were reported with telaprevir combination treatment in 4.8% of patients. Rash led to discontinuation of telaprevir alone in 5.8% of patients and 2.6% of patients discontinued telaprevir combination treatment for rash events compared to none of those receiving peginterferon alfa and ribavirin.<sup>10</sup>

Hemoglobin values of < 10 g/dl were observed in 34% of patients who received telaprevir combination treatment and in 14% of patients who received peginterferon alfa and ribavirin. In placebo-controlled Phase 2 and 3 trials, 1.9% of patients discontinued telaprevir alone due to anemia, and 0.9% of patients discontinued telaprevir combination treatment due to anemia compared to 0.5% receiving peginterferon alfa and ribavirin.<sup>10</sup>

### **About HCV**

Hepatitis C (HCV) is a blood-borne infectious disease that spreads through blood-to-blood contact, damages the liver and may impair a person's life.<sup>11</sup> While it is usually symptomless at the outset - it is the world's primary cause of cirrhosis and liver cancer<sup>12</sup>. With an estimated 150 million people infected worldwide,<sup>13</sup> and three to four million people newly infected each year, HCV puts a significant burden on patients and society.<sup>14</sup> Estimations indicate that HCV caused more than 86,000 deaths and 1.2 million disability-adjusted life-years (DALYs) in the WHO European region in 2002 (latest data available).<sup>15</sup> Chronic infection with HCV About one-quarter of the liver transplantations performed in 25 European countries in 2004 were attributable to HCV (latest data available).<sup>15</sup>

### **About Janssen**

At Janssen, we are dedicated to addressing and solving some of the most important unmet medical needs of our time in infectious diseases and vaccines, oncology, immunology, neuroscience, and cardiovascular and metabolic diseases. Driven by our commitment to patients, we develop innovative products, services and healthcare solutions to help people throughout the world. Janssen Infectious Diseases-Diagnostics BVBA is part of the Janssen Pharmaceutical Companies of Johnson & Johnson. Please visit <http://www.janssenrmd.com> for more information.

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