

## First symptomatic hepatitis C treatment in development by Phynova

The UK company Phynova, which develops novel therapeutics derived from traditional Chinese herbal medicines, claims that its anti-inflammatory treatment PYN17 could become the first symptomatic therapy for hepatitis C. It is the only drug in development for treating the symptoms of liver inflammation associated with the disease, the company said.

PYN17 is currently in a double-blind, placebo-controlled Phase IIa trial in chronic hepatitis C patients in the US for which the company expects to announce preliminary data in the fourth quarter. Dr John Efthimiou, Phynova's chief medical officer, told *Scrip* that the company had decided to pursue its larger trials in the US before conducting further trials in Europe because of the FDA's clearer guidelines on trials with botanical drug products. Guidance on placebo-controlled and dose-response studies should allow shorter development times, compared with "more hazy" advice from the EU, he said.

Hepatitis C affects 1.8% of people in the US and 170 million people worldwide. Eventually it can lead to cirrhosis, with about 5% of these patients going on to develop liver cancer. The current standard of care – pegylated alpha-interferon combined with oral ribavirin – can lead to serious side-effects including flu-like symptoms, depression and anxiety, and it often fails in patients with co-existing illnesses such as HIV and diabetes. Most R&D into new HCV drugs is aimed at reducing the virus's replication, and it is directed at the HCV protease and polymerase enzymes.

Phynova's PYN17 takes a different approach, however. Although hepatitis C patients can be without symptoms for several decades, an impaired health-related quality of life is increasingly recognised in these patients even in the absence of advanced liver disease and cirrhosis. This can include symptoms of fatigue, reduced vitality, pain and depression, said Dr Efthimiou, who hopes PYN17 can address these problems.

The product candidate contains extracts derived from four well known plants: *Astragalus membranaceus*, *Schisandra chinensis*, *Salvia miltiorrhiza* and *Silybum*

*marianum*, components of which are widely available as supplements or herbal medications in the US, Europe and Asia. Phynova says the combination of these compounds acts to reduce HCV replication rate, is antifibrotic and induces hepatic stellate cell apoptosis, although the exact mechanisms by which it works are unclear. But Dr Efthimiou believes that the candidate's multivalent mechanism of action could put it at an advantage over current anti-hepatitis C drugs. It has potential use alone, or in combination with antiviral therapy, and it does not cause the severe side-effects common with antivirals, such as Vertex Pharmaceuticals' telaprevir (VX950), which is in Phase II development.

PYN17 has already shown a good safety profile in a previous six-month, placebo-controlled Phase II trial in the UK in 43 chronic hepatitis C patients, the company said. The trial had a four-week follow-up and PYN17 was administered at a dose of 2.5g twice a day.

Improvements in health-related quality of life as well as liver inflammation on the SF36 scale and liver function tests – the primary endpoints – were seen. In addition, there was a strong trend for reducing serum ALT. It was generally well tolerated with no drug-related adverse events. Phynova also plans to start a pivotal Phase IIb efficacy study in about 240 patients in the US in the first quarter of next year to further assess the effectiveness of PYN17 in acting on these endpoints.

Graham Foster, professor of hepatology at Queen Mary's School of Medicine and Dentistry, believes that "if the early promise of PYN17 is confirmed in the larger clinical trials due to start in the US shortly then PYN17 has a very good chance of being widely used for symptomatic chronic hepatitis C".

However he acknowledged that the likelihood of its success would only be revealed once data from the larger studies were available. The company's managers "clearly believe in their product (with, in my view, good reason) and hence they are to be congratulated for moving plant-based medicines into mainstream hepatology", he added.