New phase II study supports potential of gs-9450 as new treatment option for steatohepatitis

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Results from a multinational phase II study presented today at the International Liver Congress 2010 have shown that treatment with the caspase inhibitor GS-9450 can reduce markers of liver damage in patients with non-alcoholic steatohepatitis (NASH - the most serious form of non-alcoholic liver disease) as demonstrated by reduced levels of alanine (ALT) and aspartate aminotransferases (AST), hepatic enzymes that indicate cell damage.

GS-9450, a potent inhibitor of caspases-8, -9 and -1, the intra-cellular proteins that initiate programmed cell death (or cell suicide, also known as apoptosis) in damaged cells, is a potential new treatment option for patients with NASH - a disease characterised by fat build-up in liver cells with subsequent inflammation resulting in accumulation of scar tissue (fibrosis), cirrhosis and eventual liver failure.

Professor Fabio Marra of the EASL scientific committee commented: "It is encouraging to see that GS-9450-associated reduction of apoptosis and cell damage seen in animal models has translated to a significant patient population, and seems to be consistent with a good tolerability profile in patients from a variety of countries. Further studies are needed to evaluate the action of this therapy on histology and to confirm the drug's efficacy and safety in larger patient populations."

In this double-blind, parallel-group study, patients (n=124, principally

male, mean age 45 years, with Body Mass Index (BMI) of >30kg/m2) with biopsy-proven NASH were randomised to receive 1, 5, 10 or 40mg GS-9450 or placebo once daily for 4 weeks. After 4 weeks on treatment, patients in the 40mg treatment group experienced the greatest reduction in ALT and AST levels.

At week four, linear regression of ALT versus GS-9450 dose was highly significant (p