NGM282—an engineered analogue of FGF19—shows promise in patients with primary sclerosing cholangitis

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The fibroblast growth factor 19 (FGF19) engineered analogue, NGM282, inhibits bile acid synthesis, decreases markers of hepatic inflammation, and significantly improves markers of fibrosis in patients with primary sclerosing cholangitis (PSC), according to the results of a Phase 2, multicentre, randomized, double-blind, placebo-controlled study reported today. The study, which involved 62 patients with PSC diagnosed according to EASL criteria,7 offers hope of a new medical treatment for a condition in which effective drug therapies are currently limited.

"Primary sclerosing cholangitis is a rare, inflammatory, cholestatic liver disease that is characterized by progressive fibrosis of the bile ducts and liver, and causes progressive liver dysfunction," explained Prof. Gideon Hirschfield from the University of Birmingham in the UK, who presented the results today at The International Liver Congress 2018 in Paris, France. "Liver transplantation is effective for advanced disease, but there are currently no medical treatments that have been shown to prolong transplant-free survival."

NGM282 is a non-tumourigenic engineered analogue of FGF19, an endocrine gastrointestinal hormone that regulates bile acid, carbohydrate and energy homeostasis. In an animal model, NGM282 was shown to suppress the classic pathway of bile acid production, and to inhibit fatty acid synthesis and de novo lipogenesis. NGM282 was well tolerated in a

healthy volunteer study, and the molecule has recently shown potential as a treatment for non-alcoholic steatohepatitis (NASH).

The study presented today by Prof. Hirschfield randomized 62 patients with PSC and an elevated alkaline phosphatase (ALP) level (1.5x the upper limit of normal) to receive either a daily subcutaneous injection of NGM282 at a dose of 1 mg or 3 mg, or placebo. The primary endpoint was the change in ALP from baseline to Week 12.

Although there were no significant reductions in serum ALP levels in either active treatment group compared with placebo, at Week 12 significant reductions in serum levels of alanine aminotransferase (ALT) (-40 U/L) and aspartate aminotransferase (AST) (-23 U/L) in the NGM282 3 mg/day treatment group were observed (p