Introduction:
- Steatohepatitis, or NASH (non-alcoholic steatohepatitis), consists of fat accumulation, hepatocellular degeneration and necrosis, lobular inflammation, and fibrosis.
- NASH affects up to 5% of the U.S. population and resulting liver fibrosis and cirrhosis is an increasingly common cause for liver transplantation, accounting for 7.5% transplants in the U.S.
- Recurrence of NASH in the transplanted liver is common with the development of cirrhosis in nearly 20% of patients.
- There is currently no accepted medical treatment for NASH.

Objective:
- To determine the potential use of novel complex carbohydrate drugs that inhibit galectin proteins in the treatment of NASH

Methods:
- Mouse model of steatohepatitis was developed by the Stelic Institute & Co., Tokyo, Japan.
- In this model, diabetes is induced by injection of streptozotocin and mice are fed a high fat diet, as shown below.
- STAM mice reproducibly develop steatohepatitis with the development of fibrosis and cirrhosis.

Collogen deposition was evaluated by digital morphometric analysis following Sirius Red staining. Treatment with GR-MD-02 reduced collagen deposition to normal levels whereas GM-CT-01 had a less marked effect.

Conclusions:
- STAM mice developed robust histologic findings of NASH with fibrosis.
- Treatment with galectin inhibitors GM-CT-01 and GR-MD-02 had no effect on blood glucose levels. There was no effect on body weight and no deaths in the GR-MD-02 treatment group, while 2 (out of 6) of control mice died from liver complications between 9-12 weeks.
- GR-MD-02 treatment resulted in improvement in steatosis, hepatocellular degeneration and inflammation.
- GR-MD-02 treatment prevented the development of collagen deposition in the early treatment group and reversed collagen deposition back to normal levels in the late treatment group.
- GM-CT-01 had an intermediate effect on collagen deposition.
- It is proposed that treatment with GR-MD-02 may potentially benefit patients with NASH by reduction in steatosis, necrosis, inflammation, and deposition of collagen via mechanisms that are independent of improvement in glucose tolerance.

Four Week Treatment Periods:

- Vehicle Controls
- GM-CT-01 (120 mg/kg iv 2X/week)
- GR-MD-02 (60 mg/kg iv 2X/week)