**Overview**
- Eleven repurposed drugs were tested in the STAM™ mouse model of NASH.
- Three compounds significantly reduced both NAFLD score and liver fibrosis.
- One compound (NP-135) showed superior reduction in fibrosis to Cenicriviroc.

**Methods**
- Male C57BL/6 mice received 200 μg streptozotocin SC 2 days post-birth (causing mild islet inflammation and islet destruction).
- High-fat diet ad libitum from 4 weeks of age (57% kcal fat) (causing fatty changes to the liver, NASH and fibrosis).

**Results: Experiment 1**
- NP-160 (20 mg/kg) and NP-287 (8 mg/kg) reduce NAFLD activity scores.
- NP-160 (20 mg/kg) and NP-287 (8 mg/kg) trended towards a reduction in liver damage as measured by plasma ALT and AST levels (although 31% and 25% AST and 26% AST, respectively).
- NP-287 (8 mg/kg) significantly reduced liver triglycerides (by 25%) and increased liver hydroxyproline (by 43%).

**Results: Experiment 2**
- NP-160 (40 mg/kg) and NP-135 (200 mg/kg) significantly reduce liver fibrosis.
- NP-160 (40 mg/kg) and NP-287 (8 mg/kg) trended towards a reduction in liver damage as measured by plasma ALT and AST levels (although 31% and 25% AST and 26% AST, respectively).
- NP-287 (8 mg/kg) significantly reduced liver triglycerides (by 25%) and increased liver hydroxyproline (by 43%).

**Conclusions & Future Work**
- Several repurposed compounds were screened in the STAM™ model of NASH, and a number of these compounds including NP-160, NP-135 and NP-287 showed significant reductions in both NAFLD score and liver fibrosis compared to Vehicle.
- NP-160 and NP-135 compared favourably to Cenicriviroc, a dual-CCR2/CCR5 antagonist currently in clinical trials for NASH.
- Early results suggest that the mechanism involves an anti-fibrotic effect.
- A phase 2a clinical trial is currently being planned for 2019 to assess the efficacy of the lead compound(s).

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**References**

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**Figures**
- Figure 1.1 NAFLD activity scores
- Figure 1.2 HE-stained liver sections
- Table 1.1 Biochemistry
- Figure 2.1 NAFLD activity scores
- Figure 2.2 HE-stained liver sections
- Figure 2.3 Reduction in fibrosis
- Figure 2.4 Sirius red-stained liver sections
- Figure 2.5 Reduction in hypoxia