The Diet-Induced NASH/fibrosis obese mouse

✓ A fast, costless nutritional mouse model to evaluate your drugs targeting NASH in the context of obesity and insulin resistance
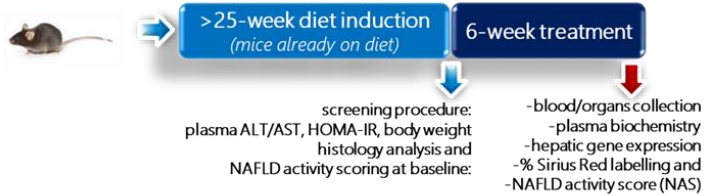
Key benefits

✓ **Get a complete evaluation** *(biochemistry, histology and NAScore) of your compounds targeting NASH in the context of obesity and insulin resistance*

✓ **6 weeks treatment to evaluate the impact of your drug vs. benchmarks**
We provide mice cohorts already on diet – our nutritional approach ensures a robust induction of obesity, NASH and portal (score 2) fibrosis and avoid the need for liver biopsies to select animals with the right phenotype
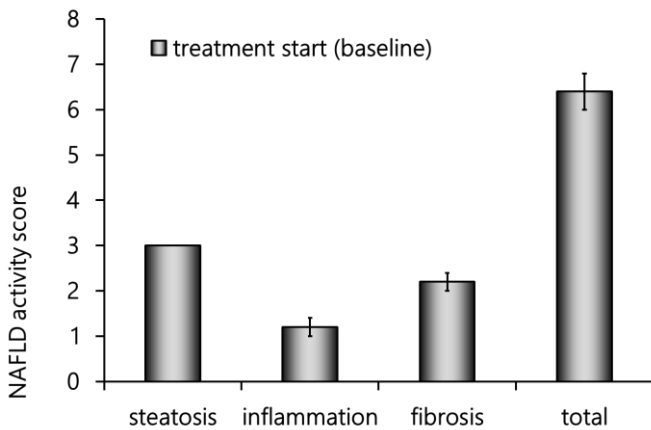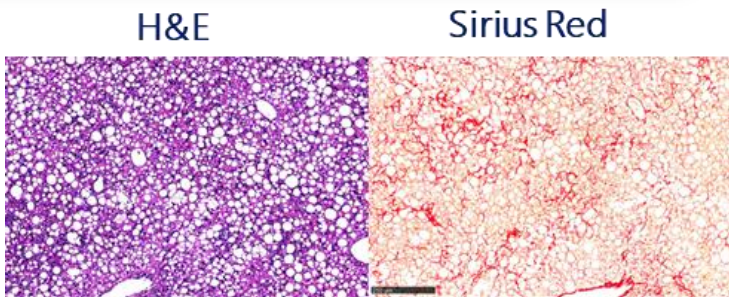
ANIMAL MODEL

- **Background strain:** C57BL/6J mouse
- **Our original diet-induced NASH:** 60% high fat diet supplemented with cholesterol + 10% fructose in drinking water
- **Study duration:** 6 weeks
- **Reference compounds:** elafibranor, obeticholic acid, semaglutide

8-week old, male, C57BL6/J mice → >25-week diet induction (mice already on diet) → 6-week treatment

screening procedure:
plasma ALT/AST, HOMA-IR, body weight histology analysis and NAFLD activity scoring at baseline:

- blood/organs collection
- plasma biochemistry
- hepatic gene expression
- % Sirius Red labelling and
- NAFLD activity score (NAS)

BASELINE CHARACTERISTICS AT TREATMENT START

H&E   Sirius Red

Representative H&E and Sirius Red staining (upper panel) and NAFLD activity score (lower panel) in mice fed with a 60% high fat + 2% cholesterol diet and 10% fructose in drinking water for 25 weeks.

6-WEEK TREATMENT WITH ELAFIBRANOR IMPROVES NASH, LIVER CELL DEATH AND FIBROSIS

vehicle   elafibranor
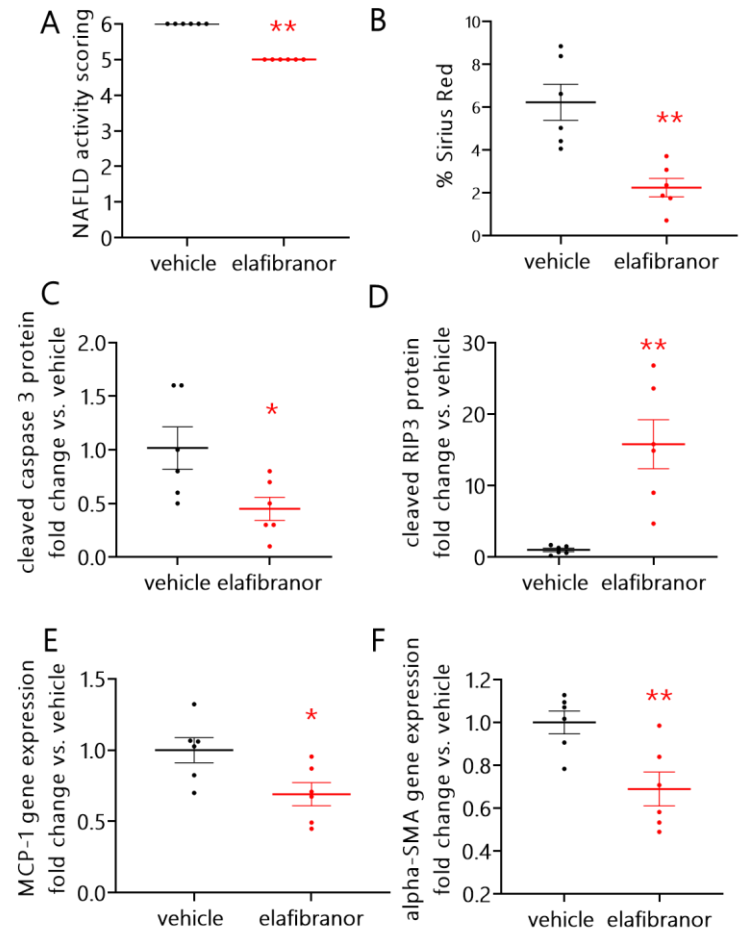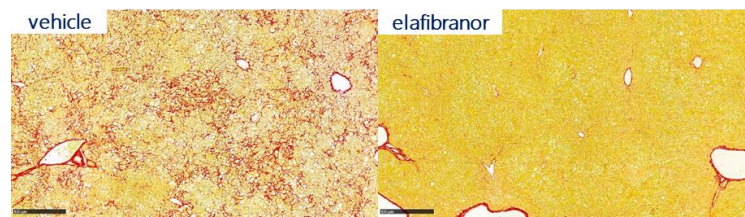
Representative Sirius Red pictures (upper panel), NAFLD activity score (A) liver % Sirius Red labelling (B), hepatic cleaved caspase 3 (C), a marker of apoptosis, and cleaved RIP3 (D), a marker of necroptosis, protein levels, hepatic MCP-1 (E) and alpha-SMA (F) gene expression in mice treated for 6 weeks with vehicle or elafibranor. $*p<0.05$, $**p<0.01$ and $***p<0.001$ vs. vehicle.