GPR84 antagonists for treatment of liver fibrosis

The Need
- Fibrosis (scarring) of the liver is a disabling effect of NASH leading to liver failure
- 1 of 8 adults have NASH, incidence of fibrotic liver diseases is high and increasing
- Many failed drugs, still no approved treatment for NASH or liver fibrosis
- There is an urgent need for effective drugs
- Market size >10B$

The Target: GPR84
- GPCR – druggable cell surface receptors
- Induced in inflammation and fibrosis
- Knockout or inhibitors protect against fibrosis
- Clinical validation from competitor compounds

Technology Description
Target
- GPR84 is a GPCR expressed in immune cells and highly upregulated in fibrosis.
- GPR84 knockout or inhibition reduces liver fibrosis in animal models.
- GPR84 inhibitors in clinic have shown effect against kidney, lung and liver fibrosis in humans

Competition
Many players in fibrosis but few companies (only 2-3) have disclosed programs on GPR84
Value proposition
- Novel small-molecule GPR84 antagonists
- Down to IC$_{50}$ = 1.3 nM - most potent GPR84 antagonist known to date
- Selected compounds show favorable physicochemical properties
Target product profile
- Oral, once daily medication that improves the outcome of patients with or in risk of developing liver fibrosis, including NASH and cirrhosis patients.

Intellectual Property Rights
Initial priority application filed 20/12-2019, PCT (WO 2021/123394) published 24/6-2021. Priority application on optimized compound series filed 18/6-2021.

Current State
We have compounds with single-digit nanomolar potency and good SAR insight from in vitro assays and favorable physicochemical properties confirmed in selected compounds
Plans for next steps include cellular studies in hepatic stellate cells, pharmacokinetic studies, and studies in rodent models of liver fibrosis.
Spin-out planned in Q2 2022.

Team
- Professor Trond Ulven
- Medicinal Chemist Loukas Ieremias
- Medicinal Chemist Asmita Manandhar
- Assoc. Professor Kim Ravnskjær
- Assoc. Professor Elisabeth Rexen Ulven

Business opportunity and Call to action
We are interested in discussions with investors that have an interest and insight in NASH, liver fibrosis and the metabolic disease area, and that could be interested in investing in a spin-out that will develop the compound series into clinical trials.

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