To determine gamma-secretase inhibitor (GSI) responder patients pan-cancer
A pan-cancer gene expression panel which can predict the sensitivity of cancer patient to multiple types of GSi compounds

The Challenge
- Oncogenic NOTCH pathway activation occurs in many cancer types, driving aggressive tumor behavior and poor patient outcome
- NOTCH signaling can be inhibited by gamma-secretase inhibitors (GSI) but clinical trial termination rates are very high due to off-target toxicities in a subgroup of patients. Robust molecular tools to enable responder patient selection for inclusion in GSI trials are needed

The Solution
- Our GSI sensitivity signature predicts large patient responder subgroups across multiple cancer types
- Our GSI sensitivity signature significantly outperforms measurements of target pathway expression in classifying sensitivity of cell lines to these drugs

Technology Description
Initially developed through analysis of bile duct cancers (O’Rourke et al. Hepatology 2020), we identified a transcriptomic signature capable of identifying GSI-sensitive versus GSI-resistant tumors.

By evaluating our GSI sensitivity signature pan-cancer (31 cancers, 9409 tumors), we predicted 41.9% of cancers to have large prospective responder subgroups (32.6% - 59.6% patients within a given cancer type) who many benefit from treatment with GSI.

In GSI-treatment screening of 60 diverse solid cancer cell lines, our 20-gene signature could discriminate nanomolar from micromolar sensitivity to GSI treatment with an AUC of 1, significantly outperforming the predictive capacity of measuring levels of individual NOTCH signalling genes.

Current State
Theranostic assay has shown predictive potential independent of solid cancer type, NOTCH mutational status and specific GSI compound (RD4929097, YO-01027, Z-LLNeoCHO). Signature has been optimized across diverse models (in vitro, in vivo, ex vivo) and technologies (gene expression array, RNA sequencing).

Next steps validation of panel in small group of GSI-treated late stage cancer patients currently, and Development of a signature-specific assay.

The Impact
- clinical development tool for GSi
- specific theranostic tool for personalised treatment strategies

Business opportunity and Call to action
We are looking for a potential licensee.