Targeting FFAR1 for Diabetes Therapy

Revitalizing a clinically validated T2D target

Biotech & Pharma

Development of FFAR1 modulators

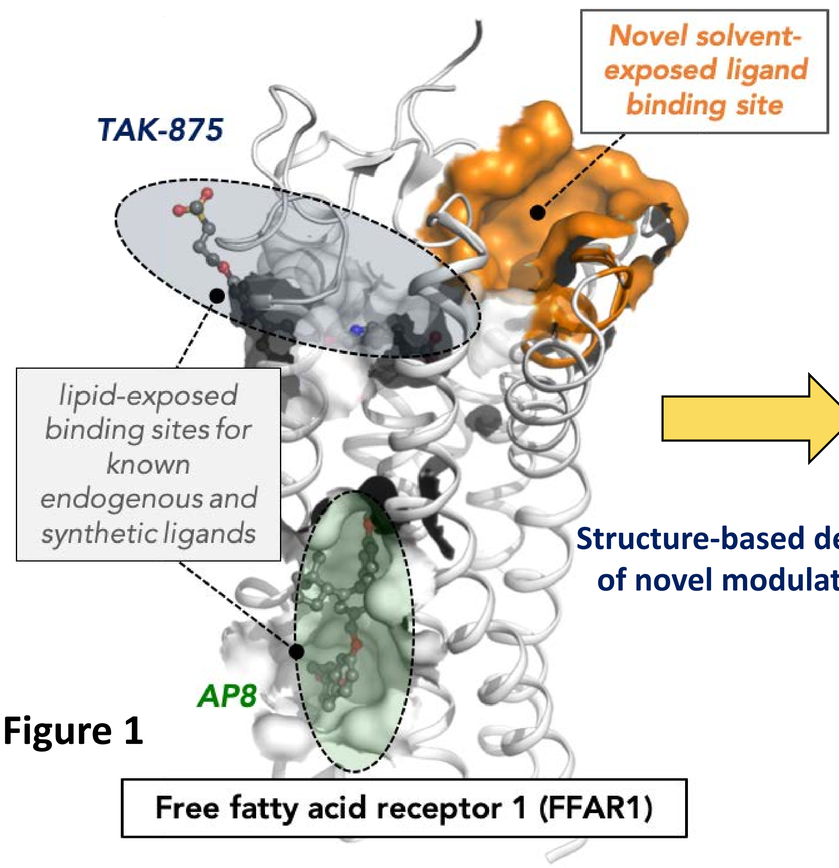


Figure 1

Structure-based design of novel modulators

Discovery of novel chemotype enabling positive modulation of endogenous signaling

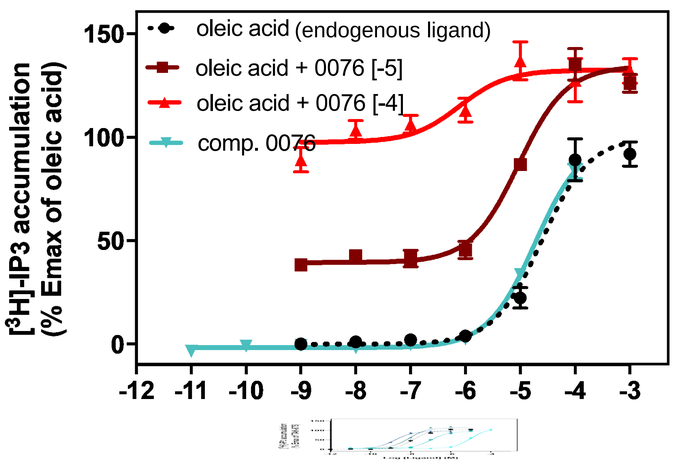
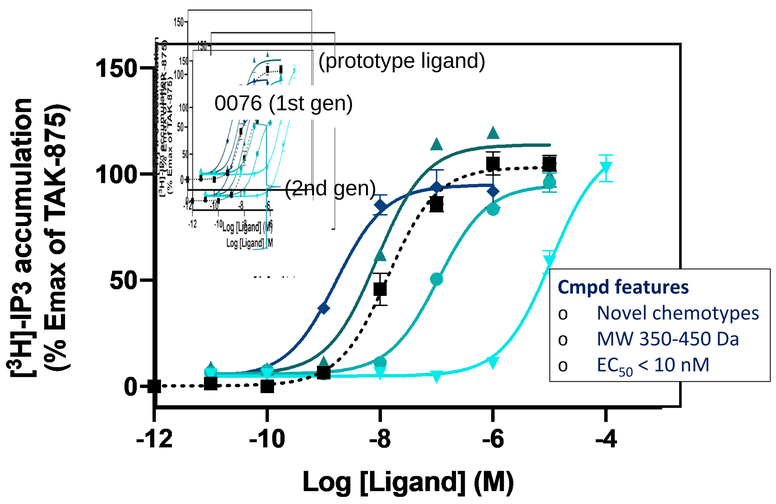
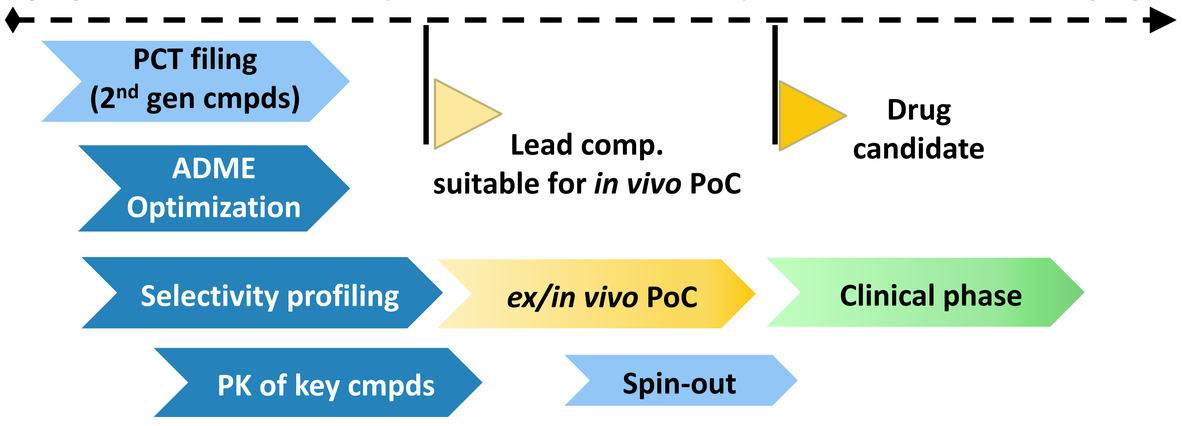


Figure 2

Synthesis and development of a SAR-rich and IP protected chemical package of novel small molecule FFAR1 allosteric modulators



Timeline and Commercialization Perspective



The global diabetes therapeutics market is forecasted to grow at a pace of ~16% a year, mainly driven by the increase of T2 diabetes prevalence worldwide. This underlines the commercial potential of novel chemotypes aiming to fulfil the therapeutic capabilities of FFAR1. The main goals for our development pipeline include:

- Medicinal chemistry optimization guided by structure-activity relationship (SAR), main ADME properties and pharmacokinetic (PK) properties
- Proof of concept (PoC) studies in animals.
- Optimize and characterize dual acting FFAR1 & FFAR4 agonists

Technology Description

Our novel modulators provide an excellent starting point to revitalize a clinically proven anti-diabetes target, the free fatty acid receptor 1 (FFAR1). This metabolite receptor is activated by long chain fatty acids to stimulate gut hormone and insulin secretion. A multitude of highly similar lipid-like ligands has been developed that act through binding to membrane lipid-exposed binding sites (Fig. 1). Traditionally, it has been notoriously difficult to develop less lipophilic and chemically attractive chemotypes for this target. We have discovered modulators with a novel chemotype combined with a beneficial signaling profile (Fig. 2). These new potential drug candidates act not only as agonists, but also as positive allosteric modulators (ago-PAMs) of endogenous free fatty acid ligands, through a new mechanism via a previously unexploited solvent-exposed binding site (Fig. 1). Optimization of 2nd generation compounds has shifted potency into the single digit nM region, while achieving significant improvements of key ADME parameters..

Intellectual Property Rights

A priority patent application was filed on November 21, 2018. A second priority patent application, covering 2nd generation compounds, was filed on May 20, 2020.

Team

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Current State

Using a combination of advanced computational chemistry and high-end-molecular pharmacology, we have designed, synthesized and experimentally tested a series of custom-made chemical mini-libraries. This has resulted in the development of a solid IP-secured chemical package of highly potent (single digit nM) and novel modulator leads with proven activity in cell-based functional assays. Further, we have validated their mode-of-action, chemical stability and established custom chemical synthesis routes for two novel scaffolds, to allow rapid chemical variations of critical areas.

Business opportunity and Call to action

We wish to attract funding to drive the further optimization of our prototype compounds. Ultimately, we seek to increase the value of the project by establishing a broad, solid industry-standard drug discovery chemical package ready for subsequent out-licensing negotiations with biotech companies and in particular the pharmaceutical industry.

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