

Lexicon and Sanofi fall out over semantics



Jacob Plieth



Citing study failure, Sanofi terminates its tie-up with Lexicon covering Zynquista; not so fast, says Lexicon, and claims breach of contract.

What constitutes a clinical study failure? The question frequently vexes biotech investors, but it could soon play out on a bigger stage. This is because its answer will determine whether Sanofi can, as it attempted to do on Friday, terminate a licensing deal with Lexicon covering the diabetes drug Zynquista.

The issue arose when Sanofi announced Zynquista's failure in one of three type 2 diabetes studies, leading the French company to serve notice to Lexicon. Lexicon, off 70% this morning, disputes this assertion, and says the notice to terminate is invalid.

Investors might well ask why Sanofi signed such an onerous deal to start with. While it is common for biopharma licensing deals to include a notice period during which the agreement can be terminated by either party, the tie-up that Sanofi signed with Lexicon in 2015 seems unusually restrictive.

According to [documents filed with the US SEC](#) at the time, Sanofi was only allowed to terminate in the event of a material breach, a material safety issue, failure to achieve positive clinical results, fundamental adverse events, or infringement of third-party patents.

It seems that only the third option applies, as both companies agreed on Friday that Zynquista was well tolerated, and no imbalances or new safety signals were observed in any of the three studies, Sota-Met, Sota-CKD3 and Sota-CKD4, in type 2 diabetes.

That said, a safety issue – ketoacidosis – did arise in type 1 diabetes, leading to a US complete response letter; but that was back in March, and prompted no action from Sanofi ([Astrazeneca and Lexicon's type 1 diabetes fortunes diverge, for now, March 25, 2019](#)). Zynquista separately has a type 1 label in the EU already.

No difference

Type 2 diabetes was key, however, because it offered Zynquista the chance of differentiation; like Invokana, Jardiance and Farxiga the Lexicon drug inhibits SGLT2. But it additionally hits SGLT1, which had been touted as a reason why it might continue to work in patients who lose renal function and no longer benefit from SGLT2 inhibition.

Friday's readouts call this into question. The crux of the matter is the Sota-CKD4 study, which enrolled subjects with severe renal impairment and which appears to have failed. Additionally, Sota-CKD3, in moderately impaired diabetics, did not show a benefit in a subgroup with more severe, stage 3B kidney disease.

Existing SGLT2 inhibitors have shown an effect in patients with mild renal impairment, so without a benefit on stage 3B and 4 kidney disease – the severe end of the scale – Zynquista’s unique selling point vanishes.

Zynquista’s latest three results in type 2 diabetes			
Study		HbA1c lowering from baseline vs placebo	Trial ID
Sota-Met	1,000 pts on background metformin	Statistically significant	2016-001800-49
Sota-CKD3	780 pts with moderate renal impairment	Stat sig in entire population & in stage 3A subjects	NCT03242252
		Not stat sig in stage 3B subpopulation	
Sota-CKD4	276 pts with severe renal impairment	Not statistically significant	NCT03242018

However, Sanofi and Lexicon disagree on whether Sota-CKD4 actually failed. Numerical data have not been revealed, but the French group states baldly that there was no statistically significant effect; Lexicon says the effect seen was “clinically meaningful ... but narrowly missed statistical significance”.

Lexicon might have a point, as Sota-CKD4 was a relatively small trial, so might have been underpowered, though strictly speaking this still amounts to a fail. The group, which says the termination is bogus and claims breach of contract, has \$133m of cash and \$250m of debt, so could have done with the up to \$430m of milestones from the tie-up.

Stifel analysts also cited Lexicon’s belief that Sanofi’s move might have been spurred by a broad plan to de-emphasise diabetes by Paul Hudson, who is set to take over as the French company’s chief executive from Olivier Brandicourt next month.

If at this point it is too late to salvage the deal, all that is to be determined is whether Sanofi will have to pay a financial penalty to Lexicon. Cue the lawyers.