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Esperion rewards the faith of IPO investors

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When the Pfizer spin-out Esperion Therapeutics floated last year it presented a simple investment case based on mid-stage studies of its sole clinical project, ETC-1002. Last night it delivered the news investors were hoping for.

ETC-1002, its oral cholesterol-lowering project, beat Merck & Co's Zetia in a phase IIb study in 348 patients, around half of whom were intolerant of statins. The fact ETC-1002 works is not much of a surprise, but its potential in statin-intolerants might afford a route to market without undergoing expensive and protracted outcomes studies – if long-term safety holds up, of course.

A positive outcome in study '008 was expected, as seen by the run-up in Esperion stock, up 35% over the past week. The biotech group had raised $78m in June 2013 when it floated at $13 a share, and a further climb of 15% in early trade today to $28 put its market cap at $430m.

In '008 the Esperion compound was pitched both as monotherapy, at 120mg and 180mg, and combined with Zetia, versus Zetia alone, in a double-blind fashion. The primary endpoint was to show a cholesterol-lowering benefit for the monotherapy versus Zetia at 12 weeks, which both doses achieved – as did the two combo doses – all with high statistical significance.

True, Zetia is hardly a difficult standard to beat, and more important is Esperion's '009 study, in which ETC-1002 is being given on top of patients' existing statin therapy, and which is due to read out in the first quarter of 2015.

But in '008 Esperion wanted to highlight ETC-1002's benefits specifically in patients with a history of statin intolerance. The '008 result, it said, shows its compound to have good tolerability and an LDL-cholesterol-lowering effect of a mid-dose statin, and stressed that efficacy was broadly the same across statin-tolerant and intolerant patients.

Intolerant edge

It is vital for ETC-1002 to show a benefit in statin-intolerant patients. Any new LDL-cholesterol-lowering project must show superiority to or differentiation from statins, and to get a broad label must additionally undergo extremely expensive multi-year cardiovascular outcomes trials.

Thus if ETC-1002 could definitively prove itself in the statin-intolerant population the long-term studies could be avoided, at least as far as initial market entry goes. Esperion is for now pitching the project carefully as a new option for patients with high cholesterol, and "especially for those with statin intolerance".

Of course, competition is hotting up here, especially from anti-PCSK9 antibodies, of which two – Sanofi's alirocumab and Amgen's evolocumab – will shortly face FDA scrutiny (*ESC – Alirocumab gives hints of great promise for PCSK9s, August 31, 2014*).

And, while ETC-1002's oral dosing gives an important edge, the PCSK9s' big pharma owners will send huge marketing forces out to make life difficult for any subsequent entrants.

Then there is the hint of additional safety issues. Some years ago the FDA decided that ETC-1002 was a potential PPAR agonist, and thus limited its human dose at 240mg and imposed additional animal toxicity trials, which will form part of any filing.

That said, the market will remember the group's history. The company was actually spun out, 16 years ago, by four Parke-Davis employees, including Roger Newton, a co-inventor of Lipitor. It was then acquired by Pfizer in 2003 for $1.3bn, but five years later Mr Newton managed to buy it out and launch it as an independent entity again.

While the clear effect of ETC-1002 on top of Zetia is important, attention now shifts to the readout of '009. Credit Suisse analysts expect an end-of-phase-II meeting with the FDA late next year, followed by the start of a phase III efficacy trial that could end in 2016/17.

Clearly, the path to market is long, though Esperion bulls will no doubt harbour alternative hopes for the company's future. Esperion is just as much a bet on the readout of additional trials as it is on Mr Newton’s proven business development acumen.

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