

Akebia plays spot the difference with investors



[Amy Brown](#)



Questions about Akebia's disclosure of liver toxicity in a trial raise a red flag over vadadustat, the company's experimental anaemia treatment.

A new description of a liver toxicity signal was all it took to knock 13% off Akebia's share price yesterday. An eagle-eyed investor spotted a shift in phraseology regarding a red flag in a vadadustat trial completed a couple of years ago, prompting [fresh fears](#) about the company's anaemia project.

At the root of the concern is what appears to be the company's first mention of Hy's law – a set of criteria used to determine whether patients are at high risk of a fatal drug-induced liver injury. Such a signal is certainly serious enough to be able to derail a clinical project, and is a good enough reason for investor skittishness.

Whether this is a legitimate concern with vadadustat is far less clear, however. Akebia had not replied to *Vantage's* questions at time of press, though notes written by sellside analysts make clear the company's defence. This signal was only seen in one subject, who went on to make a full recovery, and no other cases have been observed in the hundreds of patients treated with vadadustat; a huge pivotal programme recruiting thousands of patients is under way.

The company's stance, at least according to sellside notes, seems to be that this is not a new disclosure. Results from the trial in question were [published in 2016](#), and the safety section describes: "one patient in the vadadustat group who had an increase in liver function test, deemed possibly related to study medication."

In an [SEC filing published](#) last week the description of this event read: "one subject with multiple co-morbidities and concomitant medications, including chlorthalidone, had a serious adverse event (SAE) of liver function test, or LFT, abnormal, considered a case of drug-induced liver injury meeting the biochemical criteria of Hy's Law, which was assessed as probably related to vadadustat."

This patient's apparent ill health before receiving vadadustat is important to bear in mind here, as is the fact that regulators have allowed this project to push into thousands of other subjects, albeit with ongoing, regular safety reviews. However, possibly and probably mean very different things, and overall this second description gives the impression of a more serious situation. Investors will be keen to see that further trials confirm this liver signal as an isolated incident.

Taking a position

Vadadustat is one of three contenders in the HIF-PH space, a potentially new class of oral anaemia treatments that developers hope will prove safer and more effective than EPO drugs. Fibrogen is most advanced with roxadustat; the company is poised to publish a big analysis of the project's cardiac safety in its pivotal

programme, which could help dispel another [safety concern](#) for this class.

Akebia is already behind in development, and has much to lose here; supportive sellside analysts who spoke to the company yesterday brushed these liver safety concerns aside, variously describing the share price move as an overreaction to stale news, and recommending that investors buy the stock on the dip. These analysts, frequently defending lofty price targets on high-risk companies like Akebia, have reasons to adopt an optimistic stance in these circumstances.

It also needs to be remembered that investors with short positions have an interest in seeing shares fall.

But, as far as *Vantage* can determine, the company has yet to explain properly why the description of this liver signal has shifted so noticeably. For the sake of full and transparent disclosure investors have a right to ask this question.

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