Evaluate Vantage

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Arqule fails to stem sell-off on tivantinib safety scare

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However hard ArQule worked to play down the bad news, yesterday's announcement that patient recruitment into an Asian phase III lung cancer study of tivantinib (ARQ 197) had been halted following a safety scare caused mild panic among investors, sending the company's stock down by 19% to $5.46.

ArQule, however, remains focused on Marquee, a much bigger global pivotal trial of tivantinib that is due to undergo an interim analysis later this year, and insists that the Asian setback has no read-across into this study. Given that the company's share price has resolutely refused to be buoyed by the takeover mania that has gripped some other biotech stocks, good news with tivantinib, its lead product, is desperately needed. As such, a swift resolution of the Asian study issue, with resumption of patient recruitment, is key to proving that yesterday's sell-off was overdone.

The company said yesterday that its Asian partner, Kyowa Hakko Kirin had informed it that patient enrolment into the Attention study had been temporarily suspended following suspected cases of interstitial lung disease (ILD), a rare but potentially life-threatening complication. Patients already recruited will continue to be dosed, but the ILD cases will have to be analysed before the trial's safety review committee determines whether enrolment can resume.

Not terminal

On the face of it, this does not seem to indicate a major setback, and the study has a good chance of resuming, especially as ILD is relatively common in Japanese non-small-cell lung cancer patients on Roche's Tarceva or chemotherapy. Attention, like Marquee, is comparing tivantinib plus Tarceva to Tarceva plus placebo in non-squamous NSCLC.

But further analysis will be needed to determine how significant the reported imbalance in ILD seen between Attention's two arms is. It might also be the case that the company's relative secrecy – the setback was quietly announced in a brief filing with the SEC and not as an investor statement on its website – spooked the markets.

Analysts at Leerink Swann took heart in the fact that Marquee would continue unaffected – this trial has also been continuously monitored for safety, but no safety issues have arisen to date. They highlighted the fivefold higher incidence of ILD in Japanese versus Western patients, and said the relatively small sample size of Attention indicated a higher probability of a chance association with the active arm.

Leerink estimates that Attention had recruited around 300 of its planned 460 patients; meanwhile, Marquee completed enrolment of 988 patients in May, and is due to undergo an interim analysis for efficacy and futility after 375 events, expected later this year, with unblinding after 750 events and final data expected in mid-2013 (*Event – ArQule seeks validation to lift flagging share price, August 10, 2012*).

Most advanced project

Tivantinib is the most advanced c-Met kinase inhibitor in development for NSCLC. Consensus forecasts for 2018 in-market sales, by Kyowa in Asia and Daiichi Sankyo elsewhere, are $211m, and *EvaluatePharma* computes a risk-adjusted NPV of $829m – more than double ArQule's $340m market cap.

As analysts continue to build expectations around the interim analysis of Marquee and ArQule nurses a share price that is now back down to January levels, the Asian clinical setback is something the company could really have done without.

Study	Trial ID
Attention	NCT01377376

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