Evaluate Vantage

November 15, 2013

Despite shock adcom vote, Vanda will struggle to remain relevant

Jacob Plieth

Investing would be pointless if it were possible to predict everything accurately, so it is just as well that the US approval process can still come up with the entirely unexpected. Yesterday's overwhelmingly positive adcom vote for Vanda Pharmaceuticals' sleep disorder project tasimelteon is a case in point.

The FDA's likely approval – despite questions over Vanda's handling of clinical data – could now set a dangerous precedent and encourage post hoc data-mining by other biotechs whose R&D projects do not meet initial targets. Still, given the doubts over tasimelteon's relevance in this space, Vanda bulls would do well to use the group's 100% share spike as a selling opportunity.

The stock had surged 96% on Tuesday after briefing documents were revealed that unambiguously recommended tasimelteon's approval for non-24 sleep-wake disorder in blind people, and after the positive adcom vote it was up a further 15% this morning. Vanda's market cap is now around $430m.

Clearly the market had been expecting an adcom rejection – and for good reason. Vanda's pivotal Set study had undergone multiple revisions, including a change in its primary endpoint just before publication. The relevance of the effect was questionable, as was the fact that the new endpoint had not been validated by the FDA (*Upcoming events: FDA panel to convene over Vanda's sleep drug, November 8, 2013*).

Non-24 is a chronic circadian rhythm disorder in which the body fails to synchronise with, or entrain, the 24-hour day-night cycle, disrupting sleep and wakefulness. It occurs mostly in blind individuals, and Vanda says over half of all blind people have it.

Spanner in the works

But despite the company's claim that the US alone is home to up to 90,000 affected individuals, the disorder's definition throws a spanner in the works as far as gauging tasimelteon's market. Indeed, the high number of patients failing to meet the American Psychiatric Association's criteria had slowed recruitment into the Set trial.

Another problem is the concept of measuring "entrainment", the key efficacy endpoint under which the Set trial was eventually analysed – without any sign at that point that the FDA would accept it as a valid metric.

In the end, none of this mattered at yesterday's panel, which despite a couple of pointed questions – why not just use melatonin? Why not an alarm clock? – gave Vanda executives an easy ride.

Even the group's odd claim that tasimelteon could entrain 50% or more patients was not disputed. In the 84-patient Set trial the entrainment rate was just 20%, and though a randomised withdrawal trial entrained 90% this only looked at responders.

It is likely that the panel simply took the view that with no drugs approved for non-24, and given tasimelteon's clean safety profile, there was no reason not to approve. Market potential is not the FDA's concern, and neither are the disorder's diagnostic criteria.

The panel voted either unanimously or 10-1 in favour of all four questions: that non-24 was an appropriate indication, that entrainment was an appropriate endpoint, that tasimelteon was efficacious and that it had good safety. Tasimelteon, which has the trade name Hetlioz, now looks likely to be approved by its January 31 PDUFA date.

Déjà vu?

But the melatonin issue is pertinent. It is melatonin, a cheap nutritional supplement, that is currently recommended for treating non-24 by the American Sleep Society, and while it is not hugely effective there will be little reason to prescribe an expensive drug that offers little added benefit.

Investors with slightly longer memories will no doubt recall Vanda's schizophrenia drug Fanapt, which after a rollercoaster ride through development was deemed non-approvable by the FDA in 2008, before being approved the next year and licensed to Novartis.

In the crowded schizophrenia market Fanapt has bombed, and here is a cautionary tale for those with bullish expectations for Hetlioz. Even if the FDA follows the panel's advice and approves Hetlioz the real test will be in the market.

With dubious efficacy and the availability of cheap melatonin history could yet repeat itself.

To contact the writer of this story email Jacob Plieth in London at jacobp@epvantage.com or follow @JacobEPVantage on Twitter