Evaluate Vantage

March 30, 2016

Parkinson’s developers go one for two

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The road to US approval in a neurology indication is rarely smooth, as Acadia and Newron – two long-suffering developers of treatments for the symptoms of Parkinson’s disease – will readily testify. Yesterday their fortunes diverged.

After many regulatory twists and turns Acadia’s Nuplazid looks to be on the home straight, with a US panel endorsement for Parkinson’s psychosis. For Newron’s safinamide the agony continues: the Italian biotech yesterday earned the unenviable accolade of having received both a refuse-to-file and complete response letter from the FDA.

Though safinamide, for increasing Parkinson’s patients’ “on time”, is already marketed in the EU, the latest US delay adds a safety scare to Newron’s seeming ineptitude with paperwork, and the company was off 30% today. Acadia, which received the positive US panel vote after market close yesterday, opened up 15% this morning.

Benefits outweigh risks

One of the key considerations of the Nuplazid adcom was safety, and questions around this were far from resolved. But the fact that no other agents are available for Parkinson’s disease psychosis likely swung the debate, which ended with a 12 to two vote in favour of Nuplazid’s benefits outweighing its risks.

The panel was also satisfied that Nuplazid’s safety profile had been adequately characterised, and that Acadia had provided substantial evidence of its effectiveness, by 11-to-three and 12-to-two margins respectively. The FDA now has until May 1 to reach a verdict on approvability.

Still, while approval looks like a near certainty, attention will turn to Nuplazid’s likely label. Leerink analysts say they expect a black box warning of suicide risk, and point to discussions over a three-to-one imbalance of death versus placebo, though of course the numbers are too small to be confirmatory.

There were also questions over efficacy – to be expected given Nuplazid’s tortured development path and numerous failures (*Event – Nuplazid could finally give Acadia something to smile about, February 17, 2016*). But additional activity measures satisfied doubts over Nuplazid’s modest benefit over placebo in the single trial to yield positive data.

Given the paucity of data there were calls for Nuplazid (pimavanserin, a 5-HT2A inverse agonist) to have to undergo post-marketing trials, though Leerink reckons that the FDA will be unlikely to implement such a requirement given poor patient compliance in this setting.

EvaluatePharma sellside consensus puts 2020 sales expectations for Nuplazid at a generous-looking $838m. Having carved out a niche indication Acadia can at least have some confidence of going to market without a partner.

False dawn

Partnering deals are something that Newron does not lack, which is ironic given safinamide’s fate. Just two weeks ago Zambon sublicensed US rights to US Worldmeds – hardly a player with the clout of Abbvie or even UCB or Lundbeck, which might have been expected to be interested in licensing safinamide – but a partner nevertheless.

Zambon holds safinamide rights outside Japan, but mainly has a European presence, last year it bought the Scandinavian group Niigard to extend its marketing punch to northern Europe. But the US sublicence, triggered by FDA acceptance of safinamide’s filing, proved to be a false dawn.

Yesterday, Newron said it had been slapped with a complete response letter calling for more clinical data relating to safinamide’s abuse liability and dependence/withdrawal effects. Its assurance that there was no added requirement to demonstrate efficacy in Parkinson’s came as cold comfort.

Investors must by now be wondering whether safinamide will ever reach the US – its most important market.

Yesterday’s setback came after a filing was resubmitted a year ago and then delayed by three months; a refuse-to-file letter had come in 2014 citing paperwork irregularities.

Newron has not even provided an updated timeline for safinamide. After two private cash calls the group ended last year with €41m ($46m) in the bank, enough only to last into 2017, so it has more than one problem on its hands.

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