Evaluate Vantage

September 08, 2022

Amylyx’s fortunes shift again

Amy Brown

FDA approval of the company’s ALS project seems assured, but pledges of withdrawal on phase 3 failure come with caveats.

Amylyx could be forgiven for feeling pretty frustrated with the FDA after months of seemingly mixed messages on the approvability of its ALS project AMX0035. But, in the wake of a positive advisory committee vote, a US green light looks to be within the company’s grasp.

The regulator is due to make a decision by September 29, and Amylyx’s co-chief executives told *Evaluate Vantage* that they were not anticipating any delay. “We will be anxiously waiting, but in the meantime doing everything we can to prepare for potential launch,” Justin Klee said in an interview.

There are have been many twists in the Amylyx story, which started last year when the FDA somewhat surprisingly encouraged the company to seek approval for AMX0035 on the back of phase 2 data. And yesterday’s panel was the second for the project in the same review period, a pretty much unprecedented event.

Remarkably, yesterday also witnessed the FDA extract a public commitment from Amylyx executives that the company would withdraw AMX0035 from the market if an ongoing confirmatory pivotal trial failed.

The company said it would do so if that was the right decision for patients, and that reassurance apparently helped change some of the panellists’ minds. The first adcom ended in a 6-4 vote against, while this time that switched to 7-2 in favour of AMX0035.

That commitment comes with caveats, however.

“If [the phase 3] data suggest this is not a helpful drug for ALS then it doesn’t make sense for it to be marketed. But obviously there are lots of shades of that,” Mr Klee said. “We might find it works in subsets of patients. Or it works better in earlier stage disease. That’s why it’s important to keep studying, and we will follow the data.”

Readout of the pivotal trial, called Phoenix, is expected in mid-to-late 2024 depending on recruitment timelines, Amylyx's other chief exec, Josh Cohen, said. No other studies in ALS are planned for now, he said, meaning that a lot rests on the data that emerge from that trial.

Change of heart?

Subtle differences in the voting question also probably helped swing support in AMX0035’s favour. Rather than

having to decide whether phase 2 data established the agent's efficacy, panellists were asked whether they thought available trial evidence supported approval.

"It was a probably a much more straightforward question compared to the previous one," Mr Cohen said. New analyses of the data submitted, which the company believes more conclusively prove that AMX0035 bestows a survival benefit, also helped change minds, he said.

But interventions by the FDA's head of neurology, Dr Billy Dunn, also played a big role. As well as extracting the withdrawal pledge from the company, he emphasised that the FDA would apply the "broadest regulatory flexibility" to AMX0035's application, reminding panellists of how the disease causes sufferers to decline very rapidly.

Should approval be granted, launch could happen a few weeks later, Mr Cohen said, though he declined to commit to exact timelines. He pointed out that in Canada, where AMX0035 won approval in June, the drug was made available around six weeks later, trademarked Albrioza.

A price for the US has also yet to be decided, the chief execs said. In Canada a cost of C$17,176 ($13,000) per month was submitted to the country's health technology assessment bodies, but Mr Cohen stressed that one-by-one negotiations still had to happen with various payers.

Investors are already betting on US approval: shares in Amylyx jumped 63% in early trade this morning. Analysts at SVB Securities ramped up their probability of approval success from 35% to 75%; the bank has pencilled in sales of $1.6bn by 2026, and many on the sellside expect the agent to become a blockbuster if it reaches the market.