Evaluate Vantage

April 28, 2010

NeuroSearch data blunder dents confidence

Amy Brown

NeuroSearch, the Danish biotech that dazzled earlier this year with impressive results from a new Huntington's disease treatment, Huntexil, today lost some of its gloss. In an embarrassing disclosure, the company announced that a new analysis of the phase III data revealed the primary endpoint of the trial had actually been missed.

The disclosure cost NeuroSearch's chief medical officer his job and the company a quarter of its market value, a value that had doubled in the wake of the initial announcement (*NeuroSearch redeems itself with impressive Huntington's phase III data, February 3, 2010*). Although this certainly makes Huntexil look a riskier project than previously, this appears to be more of a statistical than a clinical glitch and stamping the trial a failure is probably a bit harsh. For faith to return, data due later this year from a phase IIb study being conducted in the US needs to be positive.

CAGn adjustment

The crux of the issue is an adjustment called CAGn, which refers to the differences in patients' genetic disposition. The company argues that this is a clinically relevant adjustment to apply to the statistical analysis of the study, called MermaiHD.

Using this adjustment, the primary endpoint of the trial was met, establishing a significant improvement in motor function in patients, with a p value of 0.02. A value lower than 0.025 was required for the trial to be judged a success.

However, the problem has arisen because this adjustment was not pre-specified as part of the protocol for analysing the data for the primary endpoint. So when the data is analysed without the adjustment, a p value of 0.042 is reached, meaning on a strict reading, the trial failed.

Reputation dent

On the upside, analysis of the secondary endpoints is unaffected and on these measures, improvement of voluntary and involuntary motor symptoms, the trial remains a success. And at the end of the day the totality of the data still points to Huntexil as potentially an important new advance for this neurodegenerative condition, for which there are precious few really effective medicines available or in development (*Therapeutic focus - Huntexil at spout of dry Huntington's disease pipeline, February 4, 2010*).

Analysts believe that should it reach the market, the product could generate peak sales of close to $1bn, globally.

On the downside, this could raise some serious questions about the credibility of the study and NeuroSearch's management. By firing chief medical officer Dr Dieter Meier the company is attempting to draw a line under the matter, but a dent to reputation might be unavoidable.

As to who knew what and when it is not clear, but being the last to know investors were understandably unimpressed. The drop in the company's share price today, which in afternoon trade was 26% lower at DKr127, no doubt reflects fears of regulatory hold ups and concern about the outcome of the second large trial, called Hart.

From the Hart

Hart is actually a phase IIb study and much smaller than the phase III, recruiting only 220 patients to MermaiHD's 437. It is also shorter, tracking patients over three months rather than six, and has more dosage arms.

The primary endpoint is the same, but some analysts have already expressed concern that due to the differences above, it is probably more likely to fail.

Coming after the re-evaluation of MermaiHD, this would not be taken well, but would not necessarily mean the end for Huntexil. In MermaiHD the drugs effects grew with time, so as long as Hart shows a trend for efficacy, it

still might be enough for regulators.

Twelve month safety data from MermaiHD is also due this year, and the company plans to file the package with regulators early next year.

If Huntexil was not intended for such a niche patient population with an extreme medical need, this news would be a lot more damaging to the drug’s prospects, and the company. As it is, unless Hart completely fails and a further phase III trial is needed the drug still has a good chance of winning approval based on the studies already being conducted. However the remaining data due this year are now even more pivotal.