Evaluate Vantage

January 03, 2013

Dexpramipexole fails to surprise in Lou Gehrig's

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Observant investors will have noticed the advertisement placed yesterday by Biogen Idec, seeking to recruit a product manager for dexpramipexole who would be a key member of the drug's launch team. But anyone hoping that this was a sign that the product's phase III Empower study in Lou Gehrig's disease was about to yield positive results was in for a nasty shock.

The data were indeed on the verge of being released, but today's announcement leaves no room for doubt as to the result: a resounding negative on primary and secondary endpoints. Even subgroup data-mining has drawn a blank, and Biogen Idec has accordingly decided to scrap development, adding dexpramipexole to the litany of failures seen so far in this intractable neurological disease.

Analysts' expectations for dexpramipexole had been very cautious, at just $122m in 2018 consensus sales forecasts and a 75% risk-adjusted NPV of $201m, according to *EvaluatePharma.* Despite this, significant sentiment had built around the project. As such the share price reaction – Biogen Idec was down 4% in early trade today – is perfectly understandable.

ISI Group's Mark Schoenebaum, for instance, had seen a favourable risk-reward balance with Empower, with a uplift from a strongly positive result far outweighing the failure downside (*Event – Amyotrophic lateral sclerosis success could empower Biogen, October 10, 2012*). Had the data shown efficacy dexpramipexole would logically have been hailed as a future blockbuster.

Resounding failure

Empower had recruited 943 amyotrophic lateral sclerosis (ALS) patients, testing 150mg of dexpramipexole (KNS-760704) twice daily versus placebo. Biogen Idec said the trial had failed in the primary measure of functional outcomes adjusted for mortality, as well as in individual components of function or survival, key secondary endpoints and analyses across multiple sub-populations.

Dexpramipexole therefore joins Trophos's olesoxime and Teva's talampanel, among others, as a recent Lou Gehrig's disease disappointment. It had been the most advanced industry project in development, and its failure leaves Mitsubishi Tanabe Pharma's edaravone and Eisai's mecobalamin as the only current phase III hopes.

Mr Schoenebaum reiterated today that dexpramipexole had carried more upside – the stock could have moved up by over 20% on a positive result – than downside – 10% – but admitted that the product was now dead. He said the Empower data had been "one of the most important 2013 catalysts" for Biogen Idec.

BG-12

Attention will now turn to dimethyl fumarate (BG-12), the Biogen Idec project widely expected to be approved and launched for multiple sclerosis in the first quarter. While this is no longer the industry's most valuable R&D asset it is potentially a huge earner, and *EvaluatePharma* puts its NPV at $11.6bn.

The immediate risk for Biogen Idec lies not in the sentiment around dexpramipexole, but in whether the failure of Empower prompts any deeper soul-searching among investors. Dimethyl fumarate, a molecule used for decades as a steriliser in the leather industry, has an awful lot to live up to as a human pharmaceutical, and were the biotech sector as a whole not riding the crest of a wave its sales forecasts would have to be seen as widely overblown.

Biogen Idec had licensed dexpramipexole from Knopp Neurosciences in 2010 for $26m up front plus a $60m equity stake. The failure of dexpramipexole, which in standalone form and in combination with racemic pramipexole for Parkinson's disease makes up Knopp's entire R&D pipeline, thus presents an uncertain future for the private company.

And we can assume that Biogen Idec will not be recruiting that product manager after all.

Study	Trial ID
Empower	NCT01281189