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Phase III data position plecanatide for grudge match with Linzess

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The future looks bright for Synergy Pharmaceuticals after the highest dose of its lead candidate, the constipation project plecanatide, met primary and secondary goals in its phase IIb/III trial. The company's share price soared 18% as a result, closing at $6.21 yesterday, adding a cool $63m to its market cap.

Synergy will surely now aim to find itself a partner to help it bring the drug to market and take a chunk out of Linzess, a potential blockbuster from Ironwood Pharmaceuticals and Forest Laboratories that has the same mechanism of action. But with plecanatide unlikely to be launched before 2015, three years after Linzess, it will have quite some ground to make up.

Dose response

The catchily named SP304-20210 trial tested three doses of plecanatide in 951 patients with chronic idiopathic constipation. Topline data showed that the highest dose of the drug, 3mg, caused a statistically significant increase in the number of complete spontaneous bowel movements (CSBMs) in 19% of patients, compared with 10.7% of those given placebo.

The number of CSBMs over the 12-week treatment period increased by 2.13 among patients in the 3mg group, a statistically significant improvement compared with the placebo group.

Only the results with the highest dose were disclosed, and the firm said that it had evidence of a dose-response. Synergy said that the data on the other two doses, 0.3mg and 1mg, would be released at a future scientific congress.

The incidence of diarrhoea seen at the 3mg plecanatide dose was 9.7%, compared with 1.3% with placebo. This is important because, though the response rate with Linzess was higher than plecanatide's, Ironwood's drug is more prone to cause diarrhoea. Linzess causes severe diarrhoea in around 15% of those who take it, and has a warning on its label to this effect.

Analysts at UBS said that the new data made plecanatide "look competitive", though a few years behind Linzess to the market. Linzess has just gone on sale in the US, having been approved last summer (*Pressure on Forest management eases with IBS pill's approval, August 31, 2012*).

IBS

Plecanatide activates guanylate cyclase type-C receptors, increasing the flow of water into the intestine. Linzess, the first-in-class guanylate cyclase-C agonist, is expected to do well, with forecast sales of $956m by 2018, according to *EvaluatePharma*'s consensus data. However, only 13% of that will come from sales in constipation, with the rest made up by its use in irritable bowel syndrome. Synergy has just initiated a phase IIb trial of plecanatide in IBS with constipation; results are widely expected to be positive.

Before plecanatide can take on Linzess, though, it must be partnered – Synergy cannot afford to market the drug itself (*Event – Plecanatide data could secure a partner for Synergy, November 15, 2012*). Synergy will be seeking to forge an alliance with a company that is ready for a fight.

Trial name	Trial ID
SP304-20210	NCT01429987

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