Evaluate Vantage

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Upcoming events – Phase III data for plecanatide and Zoptrex

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Welcome to your weekly digest of approaching regulatory and clinical readouts. Synergy Pharmaceuticals' plecanatide could be approved at the beginning of next year in its first indication, chronic idiopathic constipation, but in the meantime pivotal trials in its other use, constipation-predominant irritable bowel syndrome, will report.

Meanwhile the phase III trial of Æterna Zentaris's Zoptrex in endometrial cancer is expected to produce top-line results before the end of the year. This company has struggled to recover after a complete response letter for Macrilen at the end of 2014, and is in desperate need of some good news.

Plecanatide

Should plecanatide win approval in chronic idiopathic constipation (CIC) in January Synergy Pharma stands to make sales of $493m in 2022, according to *EvaluatePharma*'s consensus sellside forecasts. But almost the same amount – $467m – hinges on approval in constipation-predominant irritable bowel syndrome (IBS-C), so data from its two pivotal trials in this indication, expected next quarter, will be crucial.

And plecanatide is the only major late-stage constipation asset to be unpartnered; if the results are good they could prompt deal offers from larger groups.

The results of placebo-controlled phase III CIC trials, released a year ago, bode well, with the response rate similar to that seen in separate studies with Allergan and Ironwood's Linzess. Linzess, like plecanatide a guanylate cyclase type-C receptor activator, gained FDA approval for both IBS-C and CIC in 2012.

Plecanatide's safety profile was more than acceptable, with the diarrhoea rate being lower than with Linzess *(Synergy relaxes with positive constipation data, June 17, 2015)*.

There seems little reason to suspect that plecanatide will not hit in the upcoming studies too. The trials are identical, each enrolling 1,050 patients and testing two doses, 3mg and 6mg daily for 12 weeks, against placebo. The three primary outcomes are decrease in abdominal pain intensity, increase in stool frequency, and overall response – defined as a combination of the two.

Synergy will have to think seriously about a marketing partner. Valeant, previously in the frame, is no longer a realistic prospect, but with positive data it should not be too hard for Synergy to drum up interest.

Zoptrex

Æterna's Zoptrex is a peptide carrier targeting the luteinising hormone releasing hormone receptor, linked to the chemotherapy doxorubicin. It will be compared with doxorubicin alone in the phase III trial.

The ZoptEC study has enrolled 500 women with advanced recurrent endometrial cancer and looks at overall survival as the primary outcome. Last October the DSMB recommended that the trial continue after a second interim analysis on efficacy and safety at 192 events; a final analysis is expected at 384 events.

In a phase II study in 43 patients, two had complete remission while eight achieved a partial response. Median overall survival was 15 months. The Canadian company plans to file the NDA next year, with commercial launch in 2018.

Shares in Æterna have suffered massively in the past couple of years, most recently owing to Macrilen, an adult growth hormone deficiency diagnostic project, receiving a complete response letter in 2014. Shares fell 50% on the news, while back in 2012 the stock plunged 66% when phase III trials of perifosine in colorectal cancer failed.

The FDA requested a confirmatory phase III trial of Macrilen and this is due to complete in the third quarter, with the company planning to submit an NDA by the end of the first quarter of 2017.

In April Æterna signed a standby equity agreement to sell up to three million shares for up to $10m. A clinical trial success is critically needed for the company to stay afloat.

Project	Study	Trial ID
Plecanatide	First phase III trial in IBS-C	NCT02387359
Plecanatide	Second phase III trial in IBS-C	NCT02493452
Zoptrex	ZoptEC	NCT01767155

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