Evaluate Vantage

May 05, 2017

Upcoming events – Epizyme's conference data and tenapanor's pivotal results

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Welcome to your weekly digest of approaching regulatory and clinical readouts. By the summer Epizyme's tazemetostat will report data from two phase II trials in different cancers, a binary event for the epigenetic project that leads the company's pipeline.

Also the first phase III data are due for Ardelyx's tenapanor in constipation-predominant irritable bowel syndrome (IBS-C) by the second quarter. This performed well in earlier trials, although higher rates of diarrhoea remain a burden that will be monitored closely.

Make or break

Investors will get a first look at interim results from a phase II trial of Epizyme's tazemetostat in molecularly defined solid tumours when Asco abstracts are released late on May 17; Epizyme expects to discuss them on a conference call the following day. The results will be part of poster sessions at the conference on June 4.

The company will present data from a different trial at a plenary session at the International Conference on Malignant Lymphoma on June 14 in Switzerland. This ought to come from all five cohorts in its ongoing phase II study in patients with relapsed or refractory follicular lymphoma and diffuse large B-cell lymphoma (DLBCL).

Tazemetostat is an inhibitor of EZH2, a histone methyltransferase whose inhibition thought to affect gene expression – an example of epigenetics. Phase I data in 15 heavily pretreated NHL patients showed nine to have objective responses, including two complete remissions. This trial included one patient with an EZH2 tumour mutation who had failed six prior lines of therapy, yet went into partial remission after 16 weeks *(With efficacy box ticked, Epizyme faces economics question, June 22, 2015)*.

Tazemetostat is also in combination trials, including one with prednisolone in relapsed/refractory DLBCL that will be added as the sixth cohort to the ongoing phase II trial. And a dose-ranging study in first-line DLBCL with R-CHOP and relapsed/refractory patients in combination with Tecentriq should read out this year. Tazemetostat received fast-track designation in the lymphoma indication.

The project has hefty forecasts attached, with sales of $889m expected by 2022 according to sellside consensus from *EvaluatePharma*, though this is not adjusted for launch probability. Leerink analysts give a probability of success of 50% and describe the upcoming data readouts as "make or break".

The company had $242.2m in cash as of end of last December, sufficient to fund it into at least the third quarter of 2018. Epizyme bought back ex-Japan rights from Eisai in 2015, and previously promised to deliver a new partner; the data might just be the trigger it needs.

Up T3MPO

Meanwhile, the pivotal T3MPO-1 trial of tenapanor should read out by the second quarter. This double-blind study is in 629 patients with IBS-C. Subjects are given 50mg tenapanor twice a day or placebo for 12 weeks, followed by a four-week randomised withdrawal period. The primary measure is overall responder rate.

A second phase III, called T3MPO-2, is due to yield data in the second half of the year. The 26-week study is looking at the same dose as T3MPO-1, again versus placebo, with percentage of subjects with overall response for six out of 12 weeks as primary measure.

A phase IIb trial in 2015 showed the twice-daily 50mg dose to produce a significantly higher overall responder rate than placebo. The responder rate was the proportion of patients with a decrease in abdominal pain of 30% or more and an increase of at least one complete spontaneous bowel movement per week versus baseline for six or more out of 12 treatment weeks.

Diarrhoea was the most frequent adverse event in 11% of patients on the twice-daily 50mg dose, but dropout rate due to diarrhoea was low at 3.4%. Higher rates were also seen in trials in the smaller indication of hyperphosphataemia, so will be watched closely in upcoming studies *(Ardelyx runs towards next phase with*

tenapanor, February 16, 2017).

2022 forecasts sit at $320m, according to *EvaluatePharma* consensus, while $641m is assigned to partnering the asset outside the US. Ardelyx regained rights from Astrazeneca two years ago, and will be keen to secure another partner.

Project	Indication	Trial	Data expected
Tazemetostat	Adults with INI1-negative epitheliod sarcoma or relapsed/refractory synovial sarcoma	NCT02601950	May 18 conference call, Asco posters June 4, abstracts 11058 & 11057
Tazemetostat	Relapsed or refractory follicular lymphoma and DLBCL	NCT01897571	June 14 ICML
Tenapanor	IBS-C	NCT02621892 T3MPO-1	Q2
Tenapanor	IBS-C	NCT02686138 T3MPO-2	H2

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