Evaluate Vantage

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Upcoming events – Fibroid data for Obseva, as Inventiva turns to Nash

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Phase III data for Obseva's uterine fibroid project linzagolix need to prove its safety, while Inventiva tests its pan-PPAR agonist lanifibranor in Nash.

Welcome to your weekly roundup of approaching clinical readouts. The Primrose 1 study of Obseva's uterine fibroid project linzagolix, a GnRH inhibitor, will report in the second quarter, and safety will be key.

In the earlier Primrose 2 trial efficacy results with the higher dose of linzagolix in combination with hormone add-back therapy (ABT) put it on a par with Abbvie's Orilissa and ahead of Myovant's Relugolix, cross-trial caveats notwithstanding. However, the loss of bone mineral density was higher than that of competitor projects in combination with ABT.

According to Leerink analysts, Obseva reasons that bone loss could be smaller in Primrose 1, since this enrolled a higher proportion of black patients. Black women tend to have higher average body mass index, which has been hypothesised to be inversely correlated with bone loss, the analysts write.

64% of patients in Primrose 1 will be non-Caucasian, meaning that patient demographics are more aligned with competitor trials; Obseva hopes that this will allow linzagolix to produce comparable levels of bone loss.

Cross-trial comparison of GnRH inhibitors in uterine fibroids – response rates						
	Linzagolix (Obseva)		**Orilissa (Abbvie)**		**Relugolix (Myovant)**	
	Primrose 2		Elaris UF-1	Elaris UF-2	Liberty 1	Liberty 2
Dose	100mg daily w/o ABT	200mg daily*	300mg bid*	300mg bid*	40mg daily*	40mg daily*
Placebo-adjusted response rate (%)	27	65	60	66	55	57
Placebo-adjusted bone mineral density change (%)	-2.50	-1.81	-0.55	-0.55	-0.41	-0.45
Study population % black women	5%		66%	66%	41%	42%

**With ABT. Responders were defined as patients with menstrual blood loss volume of ≤80ml and ≥50% reduction from baseline in menstrual blood loss volume at 24 weeks. Source: company press releases & Leerink.*

Another aspect to look for with Primrose 1 will be the results of the lower dose without ABT. ABT is needed to counteract the menopause-like symptoms associated with GnRH inhibition, but has side effects of its own and is not advised in patients with high BMI, diabetes and cardiovascular disease.

Primrose 2 showed a 27% placebo-adjusted response rate for the low dose, which the company called "clinically relevant" at the time, saying it could open up linzagolix as a first-line treatment.

However, tiny Obseva has some catching up to do. Linzagolix is forecast to sell $211m by 2024, according to *EvaluatePharma* consensus, while GnRH inhibitors from Myovant and Abbvie are forecast to reach $445m and $408m respectively.

Inventiva's Nash bash

A trial of Inventiva's lanifibranor will report biopsy data in Nash in the first half of the year. Last year the project failed in systemic sclerosis, a multi-organ fibrostic disorder, causing Inventiva's share price to halve, and Nash is unlikely to be the company's saviour.

As a PPAR agonist lanifibranor joins the likes of Genfit's elafibranor, which itself failed a phase II study; readout from Genfit's phase III Resolve-It trial has been delayed to the second quarter. Cymabay stopped development of its PPAR agonist seladelpar in Nash after interface hepatitis was seen in liver biopsies.

Bulls will be keen to point out the differences between the projects. Lanifibranor, unlike other PPARs, hits not only the alpha and delta forms of the receptor but the gamma subunit too.

Inventiva's Nash trial, Native, tests 800mg or 1,200mg lanifibranor per day for 24 weeks versus placebo. It enrolled 247 patients, and the primary measure is an improvement of at least two points on the steatosis, activity and fibrosis score.

Lanifibranor does not have sellside forecasts assigned to it, while sales of Genfit's elafibranor are expected to reach $461m by 2024, according to *EvaluatePharma*. This figure has halved from consensus forecasts made a year ago.

Late stage PPAR agonists in development in Nash				
Indication status	**Project**	**Company**	**Type of PPAR agonist**	**Trials**
Phase III	Elafibranor	Genfit/Terns	Alpha and delta	Resolve-It, due Q2
	Lipaglyn (saroglitazar magnesium)	Zydus Cadila	Alpha and gamma	Evidences IV
Phase II	Icosabutate	Northsea Therapeutics	Alpha	Icona, interim mid year
	Lanifibranor	Inventiva	Alpha, delta and gamma	Native, due H1
	CHS-131	Coherus Biosciences	Gamma	Company has decided to pursue "strategic alternatives" for CHS-131

Source: EvaluatePharma.