Evaluate Vantage

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Obseva’s linzagolix blooms but safety questions remain

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Obseva is further behind the competition in uterine fibroids but the company’s gonadotropin-releasing hormone (GnRH) antagonist linzagolix could have the edge clinically. Results from the phase III Primrose 2 trial showed a placebo-adjusted 65% response rate for a high dose of linzagolix in combination with hormonal add-back therapy (ABT), putting it in the same league as Abbvie’s Orilissa, and slightly better than Myovant’s Relugolix, cross-trial caveats notwithstanding. The pull for linzagolix is a low dose option 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. The company described a 27% placebo adjusted response rate for the low dose as “clinically relevant”, saying it could open up linzagolix as a first-line treatment. One potential hurdle is safety: bone loss points to greater levels than with competing projects, though Obseva claims that patient demographics could explain this. A second pivotal study, Primrose 1, will need to confirm this profile for a filing to occur next year. Tiny Obseva has its work cut out to catch up in this space, however.

Cross-trial comparison of GnRH inhibitors in uterine fibroids

	Linzagolix (Obseva)		**Orilissa (Abbvie)**		**Relugolix (Myovant)**	
	Primrose 2		Elaris UF-1	Elaris UF-2	Liberty 1	Liberty 2
	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%

**Doses with ABT; bid=twice daily. Source: company press releases, Leerink.*

Responders were defined as patients with menstrual blood loss volume of less than 80mL and ≥ 50% reduction from baseline in menstrual blood loss volume at 24 weeks

GnRH antagonists in uterine fibroids			
Product	**Company**	**2024e fibroid sales ($m)**	**Indication status**
Orilissa (elagolix)	AbbVie	657	Filed in August 2019
Relumina (relugolix)	Myovant/Takeda/Aska Pharmaceutical	458	Phase III (Marketed in Japan)
Linzagolix	ObsEva	209	Phase III
Source: EvaluatePharma			