Evaluate Vantage

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Therapy focus – Abbvie moves into pole position in women's health

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The successful completion of a second phase III trial in uterine fibroids sets up elagolix, one of Abbvie's most important pipeline hopes, for a second marketing application in the coming months. Development of the asset has been incredibly protracted, but sellside analysts reckon it could yet turn into a useful sales generator, and forecasts sit at $1.2bn in 2022, according to *EvaluatePharma* (see tables below).

Whether elagolix can live up to these hopes depends on a couple of crucial issue: whether physicians and payers ultimately view the product as better than and different from existing, generic therapies, and what treatment duration regulators allow. The fortunes of a rival candidate could also prove pivotal – safety concerns around Allergan's Esmya could feasibly remove a key competitor from the market.

Esmya has been on the market in Europe for a couple of years in uterine fibroids, but new patient starts were put on hold last month, pending enquiries into liver damage. Regulators have advised that patients already on the drug should take a liver test every month – a requirement that, should it continue, would effectively wipe out Esmya's competitive chances in this space.

Four patients in Europe taking Esmya have needed liver transplants, so presumably the risks to this product are even more drastic than just regular testing.

The US FDA recently delayed its decision on Esmya, likely pending its own enquiries, and a decision is now due in August. But sales forecasts have plummeted as a result – before the scare Esmya was viewed as a similar-sized product to elagolix.

The uterine fibroids landscape – branded products only

				Sales ($m)		
Product	**Mechanism**	**Rank**	**Company**	**2018e**	**2020e**	**2022e**
Elagolix	GnRH antagonist	Phase III	Abbvie (Neurocrine)	19	220	528
Esmya*	SPRM	Marketed (EU); Filed (US)	Allergan (US & Canada)/Gedeon Richter	26	156	302
Leuplin	GnRH analogue	Marketed	Abbvie/Takeda	238	215	199
Vilaprisan	SPRM	Phase III	Bayer	-	-	187
Trelstar	GnRH analogue	Marketed	Ipsen	74	73	71
			Total incl. others	**498**	**886**	**1,547**

**Sales attributable to Allergan only. SPRM=selective progesterone receptor modulator. Source: EvaluatePharma.*

As such, the picture above could shift again should these concerns prove baseless. Allergan has said it has seen no association between its drug and liver damage in its extensive clinical programme, but the issue will remain live for some months.

Elagolix is slightly behind in uterine fibroids – Abbvie unveiled results from a second phase III trial earlier this week, confirming the agent's potential here. Both companies are hoping to convince regulators that their candidates are safe enough to move use beyond a pre-operative setting, the patient pool to which Esmya was

restricted in Europe.

Uterine fibroids and endometriosis, both characterised by heavy and painful bleeding, are driven by gonadotrophin hormones, and drug therapies seek to block the action of these hormones or downregulate their secretion. While endometriosis can in many cases by treated with hormone-based contraceptive pills, uterine fibroids represent a much tougher target, and many patients will have to undergo surgery.

Thus moving drugs into a more chronic positioning in fibroids would obviously make a big difference commercially. The length of treatment cycles that regulators permit will too; loss of bone density is the major safety concern with all of these agents and has restricted their use, though add-back hormone therapy can ameliorate this to a certain extent.

The endometriosis landscape – branded products only

				Sales ($m)		
Product	**Mechanism**	**Status**	**Company**	**2018e**	**2020e**	**2022e**
Elagolix	GnRH antagonist	Filed	Abbvie (Neurocrine)	41	344	671
Visanne	Progestogen agonist	Marketed (not in US)	Bayer/Mochida	215	239	264
Leuplin	GnRH analogue	Marketed	Abbvie/Takeda	234	212	196
Trelstar	GnRH analogue	Marketed	Ipsen	33	32	31
Zoladex	GnRH analogue	Marketed	Astrazeneca	34	32	30
			Total incl. others	**564**	**872**	**1,222**

Source: EvaluatePharma.

Treatment cycle length, and how often this can be repeated, will be a more important commercial consideration in endometriosis, which is already treated in a more chronic way – endometriosis symptoms tend to recur 9-12 months after treatment has ended with current therapies.

A 12-month versus a three-month course would provide a boost in terms of sales. With elagolix due an FDA decision in May, the verdict will provide the first window into US regulators' thoughts on this issue.

Of course there is no guarantee that these newer agents will be perceived as any safer than cheaper options by those paying the bills – the fact that regulators in Europe restricted Esmya to the pre-surgical setting in patients with uterine fibroids is perhaps telling.

But, with the future of Esmya looking shaky, Abbvie is at least in a strong competitive position. Other agents are in development, most notably relugolix from Myovant, but this is another couple of years behind. Abbvie will want to make the most of this window of opportunity.

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