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Upcoming events – Approval decision for Aclaris and Elagolix's phase III data

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Welcome to your weekly digest of approaching regulatory and clinical readouts. Aclaris could get a pleasing Christmas present in the shape of a US approval, expected by December 24, for its candidate for a skin condition called seborrheic keratosis. Current treatments are often invasive so A-101, a topical therapy, could be welcomed as an alternative.

Before the year is up phase III data are due for Abbvie's Elagolix in uterine fibroids. The project performed well in earlier trials but needs to be given alongside hormonal therapy to reduce its impact on bone density. Allergan's competing drug Esmya already has European approval, but recent reports of liver damage could give Elagolix a helping hand.

Aclaris's first FDA test

Aclaris's A-101 is a topical treatment for seborrheic keratosis, a skin condition that presents as benign, dark, textured skin growths. Prevalence increases with age, and current treatments include cryosurgery and electodessication or excision, which can be painful and prone to scarring.

A-101 is a 40% solution of hydrogen peroxide. It is designed for in-office administration and is administered using a pen-like device.

Two identical phase III trials, SEBK-301 and SEBK-302, tested A-101 versus placebo in a total of 937 patients, each with four target lesions on the face, trunk and extremities. Each lesion received one or two treatments given three weeks apart.

The trials met statistical significance on all primary and secondary endpoints. The primary measure, a significant difference over placebo on the proportion of patients achieving clearance of all four target lesions, was required by the FDA. Improved rate of clearance of three out of four lesions, the agreed European endpoint, was also met.

	SEBK-301 (NCT02667236)			SEBK-302 (NCT02667275)		
	A-101	Placebo	P value	A-101	Placebo	P value
% achieving clearance of all four target SK lesions	4.0	0.0	<0.002	7.8	0.0	<0.0001
% achieving clearance of three of four target SK lesions	13.5	0.0	<0.0001	23.0	0.0	<0.0001

There were no treatment-related serious adverse events. Local skin reactions considered greater than mild occurred in less than 1% of patients in all groups. A PDUFA date is set for December 24.

Jefferies analysts peg the likelihood of FDA approval at 85%. If A-101 is approved Aclaris plans to launch it in the second quarter of next year, targeting 3,000 high-volume aesthetic practices with its sales force of 60. JMP Securities analysts note that seborrheic keratosis affects around 83 million Americans, with 18 million seeking treatment but only eight million currently undergoing a procedure to remove the lesions, possibly due to side effects associated with existing procedures.

According to consensus from *EvaluatePharma* 2022 sales of A-101, Aclaris's lead asset, could hit $311m. As of the end of September the company had $227.8m in cash, enough to fund operations through the second half of 2019.

Elagolix takes on fibroids

Abbvie's Elagolix is an oral gonadotrophin releasing hormone (GnRH) antagonist used to treat heavy uterine bleeding associated with uterine fibroids.

Data from two identical phase III trials of the drug are expected before the end of the year. Each is testing Elagolix 300mg twice daily alone and in combination with estradiol and norethindrone acetate, known as add-back therapy, versus placebo in 400 premenopausal women aged 18-51 years old.

The primary efficacy endpoint in both trials is change in menstrual blood loss, with secondary endpoints assessing the change in fibroid volume and haemoglobin levels.

Bone mineral density will also be assessed in the studies via dual-energy x-ray absorptiometry scan. Bone demineralisation can occur if GnRH antagonists are used for long periods, and add-back therapy is used to raise oestrogen levels enough to mitigate this side-effect.

In its phase IIb study the same dose of Elagolix with and without add-back therapy met the primary endpoint of reduced heavy menstrual bleeding as compared with placebo at six months ($p<0.001$).

2022 sellside consensus for Elagolix totals $1.2bn, with 46% assigned to uterine fibroids and the remainder to endometriosis, according to *EvaluatePharma*. Elagolix originated at Neurocrine and this company is eligible for milestones and royalty payments on any future sales. It has been waiting long enough – Abbott Labs licensed the asset back in 2010 in the wake of phase IIb data.

Allergan and Gedeon Richter's Esmya is currently forecast to lead the uterine fibroids market by 2022 (see table). It initially gained approval in Europe and Canada, where it is called Fibristal, for pre-operative treatment for patients undergoing fibroid removal or hysterectomy. This approval was extended to include chronic treatment.

Allergan has filed Esmya in the US and an approval is due mid-2018. However this opportunity could now be under threat as the EMA recently started a review of the drug owing to four reports of serious liver injury, three of which ended in liver transplantation.

Top 5 uterine fibroid treatments by 2022

				Annual indication sales ($m)		
Product	**Company**	**Pharma class**	**Routes of admin.**	**2017**	**2022**	**Indication status**
Esmya	Allergan/Gedeon Richter	SPRM	Oral	112	631	Marketed, Filed in US
Elagolix	AbbVie	GnRH antagonist	Oral	-	560	Phase III NCT02654054 NCT02691494
Vilaprisan	Bayer	SPRM	Oral	-	189	Phase III
Lupron	AbbVie	LHRH analogue	Injection	178	144	Marketed
Decapeptyl/Pamorelin	Ipsen	LHRH analogue	Injection	71	71	Marketed

SPRM: Selective progesterone receptor modulator; GnRH: Gonadotrophin releasing hormone, LHRH: Luteinising hormone releasing hormone. Source: EvaluatePharma.

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