Evaluate Vantage

November 07, 2017

TherapeuticsMD closes in on FDA win

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An apparent change of heart at the US FDA means that TherapeuticsMD will be waiting for two crucial regulatory verdicts in 2018. A 32% jump in the company's shares yesterday suggests that some investors believe that success is already in the bag.

This bold bet saw TherapeuticsMD's market cap swell to $1.2bn, a weighty valuation considering that various segments of the women's health market are in the company's sights. The ignominious offloading of Sprout by Valeant yesterday serves as a reminder of the challenges of this field.

On second thought

TX-004HR is designed to treat dyspareunia, or painful intercourse due to vulvar vaginal atrophy. Having previously demanded long-term safety data the regulator has presumably decided that it will be happy with post-marketing evidence – endometrial hyperplasia was the main concern, although no signs of this were found in the company's phase III Rejoice trial.

The product is a softgel capsule that delivers estradiol, a product that is already widely prescribed to treat this and similar conditions. And herein lies the challenge for TherapeuticsMD: the market is already highly genericised and fragmented.

Amag's Intrarosa was launched in July, also for dyspareunia, while last year Amneal launched the first generic version of Vagifem – an older version of an intravaginal estradiol pill – called Yuvafem. Vagifem generated sales of $480m for Novo Nordisk at peak in 2015.

Top vaginal atrophy products

		Global sales ($m)		
Product	**Company**	**2017e**	**2022e**	**First Launch**
Premarin	Pfizer	966	893	May 1942
Yuvvexy/TX-004HR	TherapeuticsMD*	2	423	Dec 2017
Estraderm	Novartis	153	154	Dec 1985
Intrarosa	AMAG Pharmaceuticals	6	113	Jul 2017
Vagifem	Novo Nordisk	183	112	Dec 1988

**including undisclosed partner sales; source: EvaluatePharma.*

TX-004HR's pivotal trial was against placebo, so it might be difficult to judge what unique selling point it has, if any, over the generic products. This could be another case where the FDA has decided to approve a largely undifferentiated product and let the negotiations between payers and the drug company dictate uptake – it would be hard to envision another complete response letter given that the FDA has backtracked on a safety demand.

Pfizer's Premarin and generic estradiol are on the national formulary of Express Scripts, so TherapeuticsMD would likely have to offer similar terms to gain the same access, unless it can demonstrate some greater value of its offering.

Hot hot hot

TX-001HR is an oral combination pill of estradiol and progesterone in bioidentical form – the company has sought approval to treat moderate to severe menopause symptoms including hot flushes and night sweats.

Although these hormones are widely available generically, there are no FDA-approved combination products.

The sellside has bought the company's view of this opportunity – consensus currently stands at $664m in 2022 and Deutsche Bank has valued the market potential at $5bn.

TherapeuticsMD intends to partner with compounding pharmacies to help drive uptake; these pharmacies already offer the generic versions of these hormones. However, competition from widely available low-cost competition should never be underestimated.

Once again, the trials were against placebo, so it is not known what TX-001HR offers on efficacy over generics. On the other hand, the new project could have commercial advantages that TX-004HR does not – namely, convenience of a single pill along with FDA draft guidance restricting use of compounded drugs that substitute for commercially approved agents.

Still, it is difficult to see insurers paying a huge premium for what is essentially a more convenient pill. Market access, not regulatory approval, is going to be TherapeuticsMD's big challenge – investors are betting that the company is up to it.

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