Evaluate Vantage

October 31, 2019

Go or no go? Agile and Lipocine hope to make it third time lucky

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Smaller projects dominate the list, but this doesn't make them any less important for November's hopefuls.

After some huge US approvals in recent months, November is shaping up to be quieter. There are no decisions on future blockbusters set for next month, *Vantage*'s regular PDUFA analysis shows.

However, some of the upcoming verdicts will still be a big deal for the companies involved. This includes Agile Therapeutics and Lipocine, which hope to bounce back from complete response letters for the Twirla contraceptive patch and the testosterone replacement therapy Tlando respectively.

Notable first-time US approval decisions due in November			
Project	**Company**	**PDUFA date**	**NPV ($m)**
Talicia	Redhill Biopharma	Nov 2	41
Tlando	Lipocine	Nov 9	355
Fetroja/S-649266	Shionogi	Nov 14	242
Twirla/AG200-15	Agile Therapeutics	Nov 16	211
Cenobamate	SK Life Science	Nov 21	-
Exservan	Aquestive Therapeutics	Nov 30	6
Source: EvaluatePharma.			

Twirla's chances of getting approved got a boost yesterday, with an FDA advisory committee voting 14-1 that the benefits of the projects outweigh its risks – an unexpected outcome given scathing briefing documents released on Monday. The agency questioned the patch's efficacy, though Agile put unimpressive results from the pivotal Secure trial down to a high number of obese participants, in whom contraceptives do not work as well.

The FDA questioned Twirla's efficacy even in non-obese women, however, and also raised doubts about whether the project is a low-dose, and therefore potentially safer contraceptive, as Agile has claimed. Shares in the company recovered today after slumping on the briefing docs, but investors' wild ride might not be over yet.

Meanwhile, Lipocine will hope that an ambulatory blood pressure study will answer questions raised in the FDA's May 2018 CRL. The company believes that Tlando, an oral therapy, will have an edge over injectable testosterone products. Another oral contender got the FDA nod earlier this year, Clarus Therapeutics' Jatenzo, and Lipocine is embroiled in a legal wrangle with Clarus over intellectual property.

A project that should get a smoother ride is Shionogi's S-649266, or cefiderocol, a novel antibiotic targeting Gram-negative pathogens. The project recently got an adcom thumbs up, with panellists voting 14-2 in favour of approval for patients with complicated urinary tract infections and limited or no alternative treatment options.

The project has also shown promise in pneumonia. Still, as with many antibiotics, especially those saved for drug-resistant infections, succeeding commercially will be trickier.

Meanwhile, Redhill Biopharma's Talicia, which combines two antibiotics and a proton pump inhibitor, is awaiting a verdict in *Helicobacter pylori* infection. It has a good shot after a positive result in the Eradicate Hp2 trial, and a recent tie-up with Cosmo Pharmaceuticals should also give Redhill sufficient funds for launch.

However, sales expectations are not huge, with *EvaluatePharma* consensus predicting $27m in 2024.

Supplements

As for potential supplementary approvals, Lilly and Boehringer hope to get cardiovascular data on the label of their DPPIV inhibitor Tradjenta. However, the product has only shown noninferiority to placebo in the Carmelina study; with other diabetes drugs like the SGLT2s and GLP1s showing cardioprotective effects, the DPPIV class has been put in the shade.

Other decisions, including a verdict on Pfizer's Humira biosimilar, continue to be expected sometime in the fourth quarter.

The biggest regulatory event of November is not an approval but rather an advisory committee meeting, for Amarin's Vascepa. On November 14 panellists will consider the product's expanded use for the reduction of cardiovascular events in patients with high triglycerides; the FDA had previously been expected to make a call here in September.

EvaluatePharma consensus forecasts 2024 Vascepa sales of $2.2bn, but Leerink analysts believe that, if the drug does get expanded approval, US revenues could exceed $4bn.

Supplementary and other notable approval decisions due in November

Project	Company	Event type	Date
Tradjenta	Boehringer Ingelheim/Lilly	sNDA for cardiovascular risk reduction in type 2 diabetes	Nov (estimate)
Fluzone Quadrivalent	Sanofi	sBLA for influenza vaccine in pts ≥65 – high dose	Q4
PF-06410293	Pfizer	Biosimilar Humira; FDA accepted filing in Jan 2019	Q4
Xtandi	Pfizer/Astellas Pharma	sNDA for metastatic hormone-sensitive prostate cancer	Q4

Source: EvaluatePharma.