Evaluate Vantage

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Upcoming events – Sirukumab’s panel and US decision for Medicines Company

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Welcome to your weekly digest of approaching regulatory and clinical readouts. On August 2 a US FDA panel will review Johnson & Johnson’s anti-IL-6 MAb sirukumab, which if approved will enter a crowded rheumatoid arthritis market and face a battle against biosimilars (see tables below).

And in the third quarter the Medicines Company expects a US decision and phase III data for its antibiotic carbavance. This is the company’s second-biggest growth driver and is a much needed income source for a company still reeling from the patent loss of Angiomax.

Targeting IL-6

Sirukumab, which will be trademarked Plivensia, will go before an FDA panel on August 2, with an approval decision due the following month. It was filed for the treatment of adult patients with moderately to severely active rheumatoid arthritis who have failed or are intolerant to one or more disease-modifying anti-rheumatics.

Consensus sellside forecasts from *EvaluatePharma* see revenues of $1.2bn by 2022, giving the project an NPV of $5.5bn, or 2% Johnson & Johnson’s market cap. Glaxosmithkline has worldwide co-promotion rights.

If sirukumab gains approval it will become the third anti-IL-6 MAb to hit the rheumatoid arthritis market. In May Regeneron and Sanofi finally gained US approval for Kevzara – which did not have to face an adcom, but which had received a complete response letter citing manufacturing issues.

Both Kevzara and the IL-6 incumbent, Actemra, have black box warnings about serious infections, consistent with the class; this will be something to watch out for with sirukumab. Forecasts set sirukumab ahead of Kevzara but both lag behind Actemra, which has been sold since 2008.

A bigger battle against Humira biosimilars lies ahead. Last November sirukumab reported mixed results in the head-to-head Sirround-H trial against Humira, meeting only one of two co-primary endpoints. Beating Humira hands down could have given sirukumab an edge in discussions with payers.

Anti-IL-6 rheumatoid arthritis market

Product	Company	Patent expiry	2022e sales for indication ($m)	Indication status
Actemra	Roche/Chugai	28 Nov 2019	2,237	Marketed
Sirukumab	Johnson & Johnson	-	1,162	Filed
Kevzara	Sanofi/Regeneron	31 Dec 2028	647	Marketed

Source: EvaluatePharma.

Top 5 rheumatoid arthritis products by 2022				
			Global sales for indication ($m)	
Product	**Company**	**Pharma class**	**2016**	**2022e**
Humira	AbbVie/Eisai	Anti-TNFa MAb	5,627	4,693
Enbrel	Amgen/Pfizer/Takeda	TNFa inhibitor	6,357	4,097
Simponi	Johnson & Johnson/Merck & Co	Anti-TNFa MAb	1,881	2,660
Actemra	Roche/Chugai	Anti-IL-6 MAb	1,699	2,237
Xeljanz	Pfizer	JAK 3 inhibitor	927	1,670
Source: EvaluatePharma.				

Medicines Co's antibiotic

Meanwhile, the Medicines Company's carbavance is awaiting a US approval decision by the third quarter in complicated urinary tract infections (cUTI) as well as data from the phase III Tango 2 trial in carbapenem-resistant enterobacteriaceae.

Carbavance is a combination of the beta-lactam meropenem and the novel beta-lactamase inhibitor vaborbactam. The latter aims to restore potency to existing antibiotics by inhibiting beta lactamase enzymes that would otherwise degrade them.

The cUTI filing was based on the Tango 1 trial in 550 adults comparing carbavance versus piperacillin-tazobactam, another beta-lactam/lactamase inhibitor combination. After at least 5 days of IV therapy patients who met protocol-defined improvement criteria were switched to oral levofloxacin.

The study met both the FDA and EMA prespecified endpoints. The US-relevant endpoint, defined as overall success of clinical outcome in the microbiologic modified intent-to-treat population, was 98.4% in the carbavance group and 94% in the comparator group.

The second trial, Tango 2, tests carbavance against best available therapy in 150 patients with cUTI, nosocomial pneumonia and/or bacteraemia. Data are due in the third quarter, with interim results also used to support the regulatory filing.

The Medicines Company gained the antibiotic through its acquisition of Rempex Pharmaceuticals in 2013 for $140m up front. Carbavance's 2022 revenue forecasts sit at $326m by 2022, according to sellside consensus from *EvaluatePharma*, and the project is the group's second-biggest growth driver behind the LDL-lowering project inclisiran.

But the Medicine's Company is suffering from its anticoagulant Angiomax coming off patent – this had peak sales of $636m in 2014, but just $5m is forecast for 2022. The company, which is expected to see group sales fall from $684m in 2014 to $233m in 2018, along with a widening of net losses, desperately needs its pipeline to start plugging the hole.

Study	Trial ID
Tango 1	NCT02166476
Tango 2	NCT02168946

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