Evaluate Vantage

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Upcoming events – Antibiotics from Insmed and Paratek face consecutive panels

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Make-or-break FDA adcoms beckon for two antibiotics.

Welcome to your weekly digest of approaching regulatory and clinical readouts. By September 28 the FDA will issue a decision on the approval of Alis, Insmed's inhaled antibiotic. Before that, though, the lung infection drug must run the gauntlet of an adcom, set for August 7, and with Insmed seeking a broader indication than in its pivotal trial, the panel's verdict will have huge implications for the company.

The day after Alis's adcom, another will convene to evaluate Paratek's broad spectrum antibiotic, omadacycline. The product comes in both IV and oral forms and with Paratek's share price having dwindled badly in recent years the company needs a yes vote.

Alis in Wonderland

Developers of novel antibiotics have had a tough time, and the commercial struggles of those that have made it to market have cast serious doubt over whether this is an economically viable business. Still, Insmed and Paratek are two companies that have not given up.

Insmed has developed an inhaled form of amikacin, an aminoglycoside antibiotic – Alis stands for amikacin liposome inhalation suspension – as a therapy for the opportunistic infection non-tuberculous mycobacterial (NTM) disease caused by Mycobacterium avium complex (Mac). The formulation was formerly known as Arikayce.

Next week an FDA panel will assess data from the phase III Convert trial of Alis, which hit its endpoints neatly, Mac being eliminated from lung cultures in 29% of Alis-treated patients, versus 9% given usual care (*Insmed to go ask for Alis accelerated approval, September 5, 2017*).

Convert tested the drug in refractory NTM infection, enrolling 350 patients who were continually positive for Mac while adhering to a multi-drug regimen for a minimum of six months. But Insmed is seeking approval in all Mac NTM disease patients – a vastly larger population, comprising around 180,000 US patients compared with just 12,000 who are refractory, according to Stifel analysts.

The panel will probably recommend approval of Alis – the Convert results were good with a clean safety profile, and on top of that the product has orphan drug, breakthrough therapy and qualified infectious disease product status. The crucial point for Insmed is whether it will nudge the FDA to greenlight front-line use.

If it does, the company's shares should jump – though the rise might not match the 120% leap in the stock when the Convert results were released in September.

Leerink analysts, by contrast, do not expect the broader label to be recommended, noting that durability of response has only been demonstrated up to three months. Still, the need for a therapy for this infection is so pressing the panel ought to be in favour of approval of Alis in non-responders to standard of care, they write.

EvaluatePharma's consensus forecasts put 2024 sales of Alis at $642m, and if the broader label is recommended this could see an increase too.

Trial name	Trial ID
Convert	NCT02344004

If the CABP fits

On August 8 the US FDA's antimicrobial drugs advisory committee will review both forms of Paratek's broad spectrum aminomethylcycline, omadacycline – IV and oral – for treating community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI).

Paratek's filing, under priority review, is backed by three pivotal trials. The two ABSSSI studies – the Oasis-1 trial testing IV or oral formulations, and Oasis-2 with an oral-only design – showed omadacycline to be non-inferior and similarly tolerable to the gold standard, Zyvox.

Meanwhile, in CABP the Optic trial started subjects off on IV omadacycline or moxifloxacin for three to five days, before switching some to oral forms of each treatment. Like Oasis-1 and 2 this study also met non-inferiority standards according to the FDA's and EMA's respective endpoints.

Omadacycline could provide a much-needed new antibiotic option, and the two formulations mean that doctors could switch an inpatient on IV treatment to bioequivalent once-daily oral therapy on discharge from hospital. EvaluatePharma sellside consensus has the projects generating a combined $494m in 2024 sales, and Leerink analysts do not expect anything onerous at the adcom.

Positive sentiment has been driven recently by new FDA guidelines, which the company has followed. But Novartis recently became the latest big player to exit anti-infectives, and Paratek – off 70% in the past five years – could find life as a commercial player tough.

Paratek's pivotal omadacycline studies					
Study	**Use**	**Design**	**Early clinical reponse (FDA endpoint)**	**mITT & evaluable post-treatment evaluation (EU)**	**Trial ID**
Oasis-1	ABSSSI	IV to oral switch, vs Zyvox	0.7 points worse (met non-inferiority)	2.5 points & 2.8 points better (met non-inferiority)	NCT02378480
Oasis-2	ABSSSI	Oral, vs Zyvox	5.0 points better (met non-inferiority)	3.3 points & 2.3 points better (met non-inferiority)	NCT02877927
Optic	CBAP	IV to oral switch, vs moxifloxacin	1.6 points worse (met non-inferiority)	3.3 points & 2.0 points better (met non-inferiority)	NCT02531438
Source: company presentation.					