Evaluate Vantage

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Upcoming events – Anaptysbio and Retrophin await big readouts

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Anaptysbio's etokimab needs to beat Dupixent, while Retrophin takes aims at an underserved rare disease.

Welcome to your weekly digest of approaching regulatory and clinical readouts. In the second half Anaptysbio will report data from two mid-stage trials of its lead project, etokimab, which could give clues about whether the anti-IL-33 MAb could compete against Sanofi and Regeneron's Dupixent.

The most important readout will come from the Atlas study of etokimab in moderate to severe atopic dermatitis, or eczema. The primary endpoint is change in eczema area and severity index (EASI) at week 16.

The outcome for etokimab could be successful if the results are better than those seen in the pivotal eczema studies of Dupixent, although as a cross-trial comparison such findings would need to be taken with a pinch of salt.

Dupixent, an anti-IL-4 and IL-13 MAb, showed a placebo-adjusted 35-36% reduction EASI scores in its pivotal Solo-1 and Solo-2 trials.

EASI does it: can etokimab beat Dupixent in atopic dermatitis?		
	Solo-1, NCT02277743	**Solo-2, NCT02277769**
Change in EASI	35%	36%
Patients achieving EASI-75	36%	32%
Patients achieving IGA score 0 or 1	28%	27%
All data at week 16, placebo adjusted, Dupixent given every other week. Source: NEJM article, December 16, 2016.		

If etokimab can beat Dupixent on secondary endpoints, including the proportion of patients achieving EASI-75, then all the better for Anaptysbio.

Even similar efficacy to Dupixent might be passable if etokimab proves to be more convenient. Both are subcutaneous; Dupixent is given every other week, while Anaptysbio is testing various dosing frequencies for its project.

Side effects might be another area where etokimab could be differentiated, with Stifel analysts highlighting conjunctivitis as a particular area of concern for Dupixent.

Results are also due next half from the Eclipse study of etokimab in nasal polyps, another indication in which Dupixent has shown efficacy; the latter is due a US approval decision here in June.

EvaluatePharma sellside consensus puts etokimab sales at $395m in 2024, with $253m of this coming in eczema, $44m from nasal polyps, and $98m from asthma, in which Anaptysbio plans to start a phase IIb trial later this year.

If the project does not show some kind of edge over Dupixent, even these figures would be hard to hit. With Sanofi/Regeneron and Glaxosmithkline also developing IL-33-targeting projects, Anaptysbio cannot afford to slip up.

Fort building

Meanwhile, Retrophin continues to try to rebuild its reputation as a rare disease player. In the third quarter the company will report phase III data on fosmetpantotenate, its candidate for pantothenate kinase-associated neurodegeneration (PKAN).

There is no cure for this deadly neurological disorder, and patients currently receive therapies merely aimed at treating symptoms, including movement problems similar to those seen in Parkinson’s disease. Retrophin hopes that fosmetpantotenate will become the first drug approved to treat an underlying cause of PKAN, which affects around 5,000 patients worldwide.

PKAN is caused by mutations in the *PANK2* gene; this ultimately leads to a reduction in levels of coenzyme A, which plays a key role in energy metabolism. Fosmetpantotenate is designed to cross the blood-brain barrier and be converted to phosphopantothenic acid, which is involved in the synthesis of coenzyme A.

This strategy will be put to the test in the pivotal Fort trial, testing fosmetpantotenate versus placebo in 82 PKAN patients. The primary endpoint is change from baseline in the PKAN-activities of daily living scale at 24 weeks.

Retrophin’s management has said that a two-point improvement would be clinically meaningful, according to Leerink analysts, who added that a 10- to 15-point change in the similar unified Parkinson’s disease rating scale had been seen in a compassionate use study of fosmetpantotenate. However, the latter involved only four patients and did not include a placebo cohort, so Fort’s success should not be taken as a given.

If positive, the Fort trial should be enough for both US and European approval. Leerink puts the project’s peak sales at $260m, while *EvaluatePharma*'s sellside consensus has a more conservative $104m by 2024.