Evaluate Vantage

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Upcoming events: RNAi and remyelination at AAN and pivotal data from Eleven

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Welcome to your weekly digest of approaching regulatory and clinical readouts. Several companies will present data on closely watched products at the annual meeting of the American Academy of Neurology, taking place in the US capital the week after next. Alnylam will have further results from its lead neuropathy project, patisiran, Biogen will be hoping to build confidence in its anti-Lingo-1 antibody BIIB033, while GW Pharmaceuticals will give further insights into the epilepsy project driving its valuation.

Separately, in the second quarter Eleven Biotherapeutics is slated to report data from the pivotal Oasis-1 study, testing its lead project, EBI-005, in dry eye disease. The results represent a big milestone for the one-product company, which has been treading water on the stock market since it floated early last year.

AAN: April 18-25

Alnylam's RNAi therapeutic patisiran is being tested in familial amyloid polyneuropathy, a degenerative disease resulting from the deposits of amyloid fibrils on nerve cells; it is caused by mutations in the gene that codes the protein transthyretin (TTR).

12-month data from the open-label extension of a phase II trial of patisiran, or ALN-TTR02-003, will be presented. Six-month follow-up found an 80% reduction in TTR levels and stabilised neurologic impairment, and it is hoped that this signal will have been maintained over the longer period (*Study read-across and biotech bull market help Alnylam climb, October 14, 2014*).

Biogen, meanwhile, will be presenting full data from the phase II Renew trial of BIIB033, or opicinumab, in acute optic neuritis. Three months ago it emerged that Renew had missed its primary efficacy endpoint of improving optic nerve conduction velocity versus placebo in the intent-to-treat population and also in those patients who completed the full protocol, though this was a near miss (*Biogen struggles to get the Lingo right, January 9, 2015*).

Somewhat hopefully, the title of one of the five BIIB033 presentations – which describes being accompanied by a "data blitz" – suggests that the company has found evidence of remyelination with the anti-lingo-1 antibody. Whether this is in the Renew data, however, is unclear.

Finally the UK's GW is set to unveil further data from the US expanded access programme testing its cannabidiol formulation Epidiolex in a range of childhood epilepsies. The AAN meeting should see data from around 100 of the 235 children treated so far under the programme.

Back in October GW reported a 36% reduction in median seizure frequency among 58 patients who had been treated with Epidiolex for 12 weeks. With a phase III trial in Dravet syndrome recently started, investors will be hoping to see these encouraging efficacy signals confirmed at AAN.

EBI-005

EBI-005 is an IL-1 signalling inhibitor formulated for topical administration into the eye; IL-1 is a mediator that blocks several downstream inflammatory factors thought to cause dry eye disease. It represents a novel mode of action for this space, which is currently dominated by Allergan's Restasis.

Sales of that topical cyclosporine, which works by boosting tear secretions, topped $1bn last year and are forecast to grow to $1.7bn by 2020, despite tolerability problems that include ocular burning. Therefore, this space is seen as representing a valuable opportunity for improved products.

Eleven is due to report results from the first pivotal study of EBI-005. The 12-week, randomised, double-blind study enrolled 730 moderate to severe patients, who were tracked using the product in their natural environment rather than in an environmental chamber. The trial also excluded the use of rescue artificial tears.

Analysts at Leerink cite both these novel trial design factors, as well as the mechanistic logic for the targeting of IL-1, as reasons to why they believe the trial has a good chance of succeeding.

However, there are reasons for caution. The company chose to start this substantial pivotal programme on the back of only two early-stage clinical studies. Only one of these was carried out using the commercial formulation of the project; the other was run by one of the company's scientific co-founders using a compounded version. Both recruited around 75 patients.

With plans already in place to start a second pivotal dry eye study later this year and a phase III in allergic conjunctivitis, strong data will be required to build confidence in this strategy.

Study	**Trial ID**
Renew	NCT01721161
Synergy	NCT01864148
ALN-TTR02-003	NCT01961921
Oasis-1	NCT01998802

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