Evaluate Vantage

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Upcoming events – Anaptysbio targets IL-33 while Edge takes on standard of care

Joanne Fagg

Welcome to your weekly digest of approaching regulatory and clinical readouts. Anaptysbio has a busy couple of months ahead, with phase II readouts in peanut allergy and eosinophilic asthma trials testing its anti-IL-33 MAb ANB020, which has already reported positive results in a small atopic dermatitis study.

Meanwhile, Edge Therapeutics will report results from a phase III trial of its injectable version of nimodipine, EG-1962, as a treatment for complications after a burst aneurysm. This project is administered directly into the brain, and is designed to last longer and have fewer side effects than the standard of care, oral nimodipine.

Targeting IL-33

Phase IIa results for ANB020, Anaptysbio's lead asset, in peanut allergy are due in the first quarter. The double-blind, 60-day US study will test the tolerance of an oral food challenge before and after administration of a single dose of ANB020 or placebo in 20 adults with severe peanut allergy. Safety is the primary endpoint.

The second quarter will see data from a phase IIa double-blind trial in severe eosinophilic asthma. This UK study has enrolled 24 adults given a single 300mg/100ml infusion or placebo and then followed for 18 weeks. Efficacy will be assessed by FEV1.

The Californian company completed its $86m IPO in January 2017. Shares rocketed 571% over the course of last year, making Anaptysbio the biggest IPO share gainer of 2017, and valuing it at $2.5bn.

The share rally was mainly down to positive results from a small single-arm atopic dermatitis study in which 10 of 12 patients met the EASI-50 threshold, exceeding expectations. These results will need to be replicated in the much bigger placebo-controlled phase IIb study, due to start this year *(Anaptysbio adds to Dupixent pressure, October 11, 2017)*.

The company looks to be leading the anti-IL-33 space. Bigger players such as Glaxosmithkline/Johnson & Johnson and Sanofi/Regeneron also have assets in phase II, but these trials will not report until next year.

Anti-IL-33 MAbs in development, all phase II

Project	Company	Lead indication(s)	Trial ID(s)	Data?
ANB020	Anaptysbio	Atopic dermatitis, peanut allergy, eosinophilic asthma	EudraCT 2016-002539-14, NCT02920021, EudraCT 2017-000647-40	AD reported, peanut Q1, asthma Q2
GSK3772847A	Glaxosmithkline/J&J	Moderate to severe asthma	NCT03207243	Primary completion Feb 2019
SAR440340	Sanofi/Regeneron	Moderate to severe asthma	NCT03387852 (in combination with Dupixent)	Primary completion Sep 2019

Source: EvaluatePharma, Clinicaltrials.gov, Clinicaltrialsregister.eu.

Having an Edge

The Newton 2 phase III trial of Edge's lead project, EG-1962, has enrolled 374 adults with aneurysmal subarachnoid haemorrhage (aSAH), a bleed on the surface of the brain caused by a burst aneurysm. EG-1962, a formulation of nimodipine microparticles injected into the brain, is being compared with oral nimodipine.

Nimodipine is a calcium channel antagonist that works by relaxing narrowed blood vessels in the brain. The

oral version is the standard of care to prevent brain tissue death and is normally given post-surgery and within 96 hours of aneurysm rupture. Oral nimodipine is administered every four hours over a 21-day period, but is associated with hypotension, which can exacerbate the complications of aSAH.

EG-1962 is administered via an external ventricular drain, which aSAH patients normally have in place to monitor intracranial pressure. In Newton 2 subjects in the experimental arm received a single 600mg intraventricular injection of EG-1962 plus placebo capsules administered for up to 21 days. Patients in the active comparator arm received a single dose of intraventricular saline and up to 21 days of oral nimodipine.

The primary measure is the proportion of patients scoring six to eight on the extended Glasgow outcome scale (GOSE; 1 is dead, 8 is resumption of normal life) at day 90. Secondary measures include neurocognitive outcomes, safety and health economic endpoints.

A futility analysis completed at the end of last year in 150 patients, with an interim analysis from 210 patients due in the coming months. Leerink analysts note that to succeed at the interim look EG-1962 needs to be around 20% better than the oral treatment on the primary endpoint, and this could allow for early termination of the study.

Phase I/II results look promising. In the earlier 73-patient trial, 60% of patients treated with EG-1962 had scores of six to eight on the GOSE scale at 90 days, compared with 28% in the oral group. No patients in the EG-1962 group experienced hypotension versus 17% in the oral nimodipine group.

The median length of stay in intensive care was reduced by 3.5 days (20%) in the EG-1962 group versus the oral group. Meanwhile, delayed cerebral ischaemia, the most important cause of morbidity and mortality in patients surviving the initial rupture, was reduced by 61% with EG-1962.

The project has US and EU orphan drug designation. In the US Edge plans to use the shortened 505(b)(2) regulatory pathway. *EvaluatePharma* sellside consensus forecasts EG-1962 sales of $417m by 2022.

To contact the writer of this story email Joanne Fagg in London at joannef@epvantage.com or follow @ByJoFagg on Twitter