Evaluate Vantage

September 22, 2017

Upcoming events – Spark's FDA panel and Alzheimer's data for Biogen and Eisai

Elizabeth Cairns

Welcome to your weekly digest of approaching regulatory and clinical readouts. Luxturna, Spark Therapeutics' gene therapy for a rare eye disorder, will be up before an FDA panel next month, and as the condition in question is untreatable regulators might come under pressure to look favourably on the project.

Before the end of the year Eisai and Biogen will report topline phase IIb data for their Alzheimer's MAb BAN2401, which targets amyloid fibrils. This is a high-risk therapy area, home to clinical setbacks aplenty.

Sparks might fly

Luxturna (voretigene neparvovec) is intended to treat biallelic RPE65-mediated inherited retinal disease, a group of disorders that can lead to blindness.

Its phase III study tested 31 patients with Leber's congenital amaurosis (LCA) type 2 who had confirmed RPE65 mutations. Luxturna was injected subretinally into both eyes during surgeries on separate days in patients aged three and older.

The study met its primary endpoint, a statistically significant difference in multi-luminance mobility testing at one year, which tests ability to navigate a marked path while avoiding obstacles in or adjacent to the path, in varying light levels, an endpoint developed by Spark with FDA input.

Two secondary endpoints were met, but the change in visual acuity averaged over both eyes was not significant (p=0.17). Spark said improvement here was not necessarily expected as visual acuity is a measure of cone-mediated function, and LCA is a rod-mediated disease.

The US advisory panel will convene on October 12, with a PDUFA due in January. Luxturna's US orphan drug designation also covers RPE65-mediated retinitis pigmentosa, although trials have not yet been started in this population.

It is difficult to predict how the FDA will view the data as there is no precedent for the condition; the route of administration, along with the need for general anaesthesia, will also have to be weighed up. If Luxturna is approved next year it could become the first gene therapy to get the green light for a genetic disease in the US.

Luxturna is Spark's lead project, and its 2022 sales are forecast at $371m by sellside consensus from *EvaluatePharma*. Questions will linger over its price if it is approved, with Leerink analysts modelling $600,000 per patient in the US and $400,000 in Europe. While Novartis's recently approved CAR-T product Kymriah is priced at $475,000, there is no charge if the patient does not respond by the end of the first month after treatment.

Protofibril MAb

Meanwhile, phase IIb data are due with BAN2401, a MAb that binds to beta-amyloid protofibrils that was originally developed by Bioarctic before being licensed to Eisai, which then signed an agreement with Biogen.

The phase IIb study in question, which Eisai expects to serve as one of two pivotal trials, has a Bayesian adaptive design. This means that there are frequent interim analyses to update randomisation of patients, assigning more to the doses that appear more efficacious and fewer to those that are less effective.

It enrolled 856 patients with mild cognitive impairment owing to Alzheimer's disease or mild Alzheimer's disease dementia, and comprised five active arms with three doses, up to 10mg/kg, given once every two weeks and two doses given monthly, versus placebo.

Before the end of the year, interim results are expected from its primary endpoint, change from baseline in the Alzheimer's disease composite score – a measure of cognition and function – at 12 months. And by the middle of next year the full analysis of the endpoint at 18 months will be reported.

Hippocampal volume, assessed by MRI, and changes in amyloid levels, assessed by PET imaging, are secondary endpoints.

In July an independent monitoring committee recommended continuation of the study after a nine-month analysis of 800 patients. BAN2401's sales forecasts sit at $151m by 2022, according to *EvaluatePharma*.

Biogen's other Alzheimer's MAb, aducanumab, to which Eisai has a joint development and commercialisation option, is forecast to be its biggest seller by 2022, but as phase III data are not due for another couple of years. Alzheimer's remains an elusive bet.

Top 10 Alzheimer's products by 2022

			Annual indication sales ($m)				
Product	**Company**	**Pharmacology class**	**2016**	**2018**	**2020**	**2022**	**Current status**
Aducanumab	Biogen	Anti-beta-amyloid MAb	-	-	181	1,536	Phase III
Intepirdine	Axovant Sciences	5-HT6 antagonist	-	2	474	1,013	Phase III
Verubecestat	Merck & Co	Beta secretase cleaving enzyme 1 inhibitor	-	-	90	305	Phase III
Elenbecestat	Eisai	Beta secretase cleaving enzyme inhibitor	-	-	15	284	Phase III
Aricept	Eisai	Acetylcholinesterase inhibitor	455	313	247	217	Marketed
Namzaric	Allergan	Acetylcholinesterase inhibitor & N-Methyl-D-Aspartate receptor antagonist	58	187	216	203	Marketed
Exelon	Novartis	Acetylcholinesterase & butyrylcholinesterase inhibitor	366	337	238	182	Marketed
Reminyl	Takeda	Acetylcholinesterase inhibitor	161	179	179	165	Marketed
Memary	Daiichi Sankyo	N-methyl-D-aspartate receptor antagonist	434	495	359	155	Marketed
BAN2401	Eisai/Biogen	Anti-beta-amyloid protofibrils MAb	-	-	15	151	Phase II

Source: EvaluatePharma.

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