Evaluate Vantage

July 08, 2020

US regulator finally grasps aducanumab

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After first pledging to file aducanumab in early 2020 Biogen today revealed that it had only now submitted the controversial Alzheimer's disease project to the US FDA, sending shares up 5%. The FDA now has 60 days to accept or reject the filing and decide whether to grant priority review. And here lies the rub: there are questions around Biogen's data package, including missing data values and a less than convincing efficacy profile. An advisory committee will no doubt be called to scrutinise the toxicity profile and statistical rigour of aducanumab's clinical programme. However, given the paucity of Alzheimer's treatments and an FDA that has shown leniency towards treatments for intractable diseases with no other options, aducanumab's filing looks likely to be accepted. Beyond aducanumab Biogen's pipeline is thin, and a patent loss for Tecfidera last month deepened the company's reliance on the Alzheimer's project. Roche and Lilly have both spent years trying to gain ground with their own beta amyloid-targeting MAbs, and will surely keep a close eye on the regulator's proceedings.

Aducanumab's phase III dataset (high dose)		
	Emerge	Engage
	n=547	n=555
CDR-SB (original primary endpoint)		
Reduction vs placebo	-22%	2%
Nominal p value	0.01	0.833
Adas-Cog (one of 3 secondary endpoints)		
Reduction vs placebo	-27%	-11%
Nominal p value	0.01	0.258
Source: 2019 CTAD presentation.		

Beta amyloid MAbs in late-stage development				
Project	**Company**	**Indication sales 2026e ($m)**	**Disease setting**	**Note**
Phase III				
Aducanumab	Biogen/Eisai	2,894	Early/mild	Completed FDA filing based on two phase III studies, Emerge and Engage, and phase Ib Prime
BAN2401 (lecanemab)	Biogen/Eisai	969	Early	Clarity AD study due to report in 2022
Gantenerumab	Roche	69	Early	Graduate 1 and 2 studies, primary completion 2022
Solanezumab	Lilly	-	Asymptomatic	A4 study, primary completion 2022
Phase II				
LY3002813 (donanemab)	Lilly	22	Early	Trailblazer-Alz, data due Jan 2021
Crenezumab	Roche/AC Immune	-	Autosomal dominant	NCT01998841, primary completion 2022
Source: EvaluatePharma, clinicaltrials.gov.				