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The aura of success surrounds Allergan’s oral migraine data

Jonathan Gardner

Botox maker Allergan has been somewhat overlooked in the battle to launch novel migraine agents. Its two-pronged approach to bringing CGRP-blocking pills to the market could figure more prominently in investors’ views, however, now that the episodic treatment atogepant scored a statistically significant improvement over placebo at five different doses in a phase IIb/III trial.

With a benefit that looks on a par with Amgen’s Aimovig and other anti-CGRP antibodies, atogepant must be viewed as a serious competitor. Oral delivery may make it more attractive to patients, while as a small molecule it has the potential to be priced below biological drugs, which could allow Allergan to take market share.

These data follow the completion of Allergan’s clinical programme for utogepant, which as an acute migraine therapy would compete mostly with triptans and standard analgesics. The New Jersey-based company plans to submit that pill to the US FDA for approval in 2019.

Looking safer

With a longer half-life than utogepant, atogepant is intended as a preventive treatment, as are the anti-CGRP antibodies. The challenge was developing a daily oral medication that had acceptable safety as earlier candidates in this class, Merck & Co’s telcagepant and MK-3207, had shown increases in liver enzymes. It is notable that Merck & Co more or less gave up development of a 'gepant and licensed its remaining assets to Allergan.

Atogepant passed the liver test, with only eight of the 639 patients who received it in the trial having liver enzyme elevations above three times the upper limit of normal, and only one of those exceeding five times the upper limit of normal. Evercore ISI analyst Umer Raffat described the results as “very clean”.

On efficacy, at five different dose levels atogepant managed to reduce monthly migraine days by between 0.7 and 1.39 when compared with placebo. All doses resulted in statistically significant improvements. By comparison, in the episodic setting – for patients with up to 14 headache days a month – Aimovig reduced headache days by 1.3 and 1.9 days for the 70 and 140mg doses, respectively, when compared with placebo.

Pivotal design

With liver toxicity a concern in atogepant’s class, it seems likely that the FDA would favour as low a dose as possible – fortunately for Allergan, the lowest dose of 10mg once daily had the strongest p value of any of the doses tested. One other question to be resolved is Allergan’s use of “migraine/probable migraine days” as the primary endpoint – Mr Raffat wrote today that makers of anti-CGRP antibodies measured “probable migraines” in pivotal trials, but only as secondaries.

Leerink analyst Geffrey Porges took a cautious view of the atogepant data, pointing out that larger patient numbers will be necessary to assess how it will stack up against the biological CGRP agents. He added that he believes the chronic populatio, or those with 15 or more headache days a month, is the more meaningful commercial opportunity.

Allergan believes it might be able to persuade the FDA to allow this trial to be one of its two pivotal studies necessary for approval. In parallel, it is expected to test atogepant in the chronic setting.

Safety concerns have likely kept atogepant’s forecasts modest as it has progressed through the clinic. These data should remove some of those worries – and if they are gone for good, its prospects will come down to how it stacks up against biologicals on efficacy, and how pricing could affect payer preferences.

CGRP-targeting agents in migraine									
			WW sales ($m)						
Product	**Company**	**2018e**	**2019e**	**2020e**	**2021e**	**2022e**	**2023e**	**2024e**	**WW Phase**
Aimovig	Amgen/Novartis	138	447	845	1,213	1,483	1,735	1,928	Markete
Galcanezumab	Eli Lilly	39	173	325	486	622	746	860	Filed
Fremanezumab	Teva Pharmaceutical Industries	2	105	243	374	522	672	797	Filed
Eptinezumab	Alder Biopharmaceuticals	-	53	105	240	416	603	789	Phase III
Ubrogepant	Allergan	-	-	51	148	271	390	487	Phase III
Atogepant	Allergan	-	-	-	-	39	96	146	Phase III
Source: EvaluatePharma									

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