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Alder on a Promise, but it could be too late

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Alder Biopharmaceuticals needed a hit in Promise 2, the second phase III trial of its migraine candidate eptinezumab, to file the asset this year. A hit has duly arrived, and unlike the lukewarm showing in the episodic setting that emerged in summer the data were good enough to send the company's shares up 12% on the news.

Decent though the results are, they might have come too late. Three potential competitors have already been filed with the FDA, and Alder will be a year or so behind in a sector where first-mover advantage is seen as crucial.

In Promise 2, conducted in 1,072 chronic migraine subjects, eptinezumab reduced the number of monthly migraine days from baseline by 8.2 at 12 weeks, significantly better than the 5.6-day reduction with placebo. This 2.6-day difference makes it the best of the CGRPs in the chronic setting – but only very marginally, and in the absence of a head-to-head study Teva's fremanezumab must be viewed as pretty much equally effective.

And fremanezumab is already with the regulators – along with Amgen and Novartis's erenumab and Lilly's galcanezumab. Since all three antibodies can point to greater reductions in monthly migraine days in episodic migraine patients than Alder's candidate, it will have to make all it can of its tiny advantage in the chronic setting.

Phase III results of anti-CGRPs

Project	Company	Migraine type	Efficacy vs placebo	Study	Study ID	Status
Aimovig (erenumab)	Amgen/Novartis	Episodic	1.1 days	Arise	NCT02483585	PDUFA for chronic and episodic May 17, 2018
		Episodic	1.4-1.9 days	Strive	NCT02456740	
Fremanezumab (TEV-48125)	Teva	Episodic	1.5 days	Halo EM	NCT02629861	PDUFA for chronic and episodic due mid 2018
		Chronic	2.5 days	Halo CM	NCT02621931	
Galcanezumab	Lilly	Episodic	1.8-1.9 days	Evolve-1	NCT02614183	Filing accepted Dec 2017
		Episodic	1.9-2 days	Evolve-2	NCT02614196	
		Chronic	2 days	Regain	NCT02614261	
Eptinezumab	Alder	Episodic	0.7-1.1 days	Promise	NCT02559895	Filing expected in second half of 2018
		Chronic	2.6 days	Promise 2	NCT02974153	

The company did not detail the results seen with the different doses in Promise 2. Eptinezumab was delivered as a single infusion, with patients receiving 300mg or 100mg, or placebo.

Alder money in the world

Alder's share price rise is perhaps not entirely attributable to Promise 2. The company also put an end to litigation with Teva, agreeing a European patent settlement and licence with the Israeli group. The non-exclusive global licence to Teva's CGRP portfolio covers all countries except Japan and South Korea.

This agreement calls for Alder to make an immediate payment to Teva of $25m. It will hand over another $25m on first approval of eptinezumab anywhere in the licensed territory.

It will pay these fees with the proceeds of an equity sale. It has sold $100m of Class A preferred stock to institutional and other investors affiliated with the hedge fund Redmile Group. Each of these Class A shares is convertible into 10 shares of Alder's common stock if certain conditions are met. The cash will also go towards launch preparations.

The licence will also see Alder pay Teva $75m when eptinezumab's annual sales hit $1bn, and again when they hit $2bn. Given that the drug's 2022 sales forecast sits at $394m, according to *EvaluatePharma*, Teva might have some time to wait for this cash.

At least the approval ought to arrive. But, unless something goes awry with one or more of the other three competitors' applications, Alder seems destined to be fourth to market. At that point seizing market share might be tricky, particularly with undistinguished clinical data.

This story has been updated with the filing date of galcanezumab.

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