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Marginal migraine benefit puts Amgen and Novartis in pole position

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A positive readout for erenumab in chronic migraine positions Amgen and Novartis to be first to market with a CGRP-targeting antibody, assuming that two pivotal studies in the episodic form of the disease, due later this year, mirror earlier results.

First-mover advantage will be important, given that Lilly, Alder and Teva are hot on the heels of erenumab with similarly acting projects that so far have generated similar levels of efficacy. However, the pricing argument might be difficult since the benefit – a relative reduction of barely two migraine days a month – seems clinically unimpressive (see table below).

To be sure, statistically the data are significant. But Novartis and Amgen are again showing that, on average, patients on treatment are still experiencing migraine attacks almost every other day; a careful argument will need to be made to persuade payers that this represents a significant improvement in quality of life.

Reducing migraine days

The data with erenumab (previously known under the lab code AMG 334) came from a phase II trial in 667 chronic migraine patients experiencing on average 18 migraine days a month.

Each erenumab dose (70mg and 140mg) cut this to about 11.4 days a month, while patients on placebo saw their migraine days cut to some 13.8 days. The placebo response seems high, though not out of the ordinary, and the relative benefit is just 2.4 days – similar to competing projects, with the caveat of across-study comparisons.

Amgen and Novartis said the result was statistically significant but did not reveal the level of significance. Evercore ISI's Mark Schoenebaum added that the apparent lack of a dose response was "interesting", and would need more investigating with presentation of detailed data and responder rates.

CGRP-targeting antimigraine MAbs

Company	Project	2022e sales*	Target	Migraine type	Status	Efficacy**
Amgen/Novartis	Erenumab	$269m	CGRP receptor	Episodic	Phase III	1.1 days
				Chronic	Phase II	2.4 days
Lilly	LY2951742	$387m	CGRP ligand	Episodic	Phase III	1.3 days
Alder	ALD403	$821m	CGRP ligand	Episodic	Phase III	1.0 days
				Chronic	Phase II	2.8 days
Teva/Rinat	TEV-48125	$1,069m	CGPR ligand	Episodic	Phase III	1.7-2.0 days
				Chronic	Phase III	2.6-2.8 days

*Note: *EvaluatePharma sellside consensus; **reduction in monthly migraine days vs placebo. Source: Evercore ISI, Bernstein.*

The CGRP-targeting migraine space has seen a resurgence over the past year, with Allergan licensing two Merck & Co assets, and Teva and Heptares striking an early research alliance, shortly after Novartis tied up with Amgen on erenumab (*Therapy focus – Another bet on the small-molecule approach to migraine, November 26, 2015*).

This activity makes Alder particularly interesting: the young biotech listed two years ago and is the only small company working on CGRP inhibition without a partner. It has fallen over 30% since last July's market peak, and with a market cap of just $1.5bn could feature in deal bankers' pitches if its data hold up.

Like Amgen and Novartis, Alder will have to work hard to make out the case for a meaningful clinical benefit. The developers might for instance look at overall efficacy, irrespective of placebo response, and tease out responder data to show how some patients experience an effect far above the average.

With erenumab's phase II chronic data in, the focus turns to two phase III trials in episodic disease: Arise in 577 patients and Strive in 955. Amgen previously said it would file all the available data in one package, and the two pivotal trials are due to read out the second half.

This suggests that yesterday's phase II study could be relied on as part of a combined regulatory package for episodic and chronic migraine. Whether it is enough, or whether an additional phase III trial in the chronic setting is needed, will be down to the US FDA.

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