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May 21, 2015

Event – Amgen and Sanofi face final check before start of PCSK9 chase

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It is uncommon in pharma to see as straight-up a horse race as that facing the cholesterol-lowering agents Praluent from Sanofi and Regeneron and Repatha from Amgen – the two PCSK9 projects could be launched in the US within weeks of each other later this summer. A two-day FDA advisory committee next month will shed light on what differentiation, if any, there is between them.

Given that long-term outcomes data will not be available until 2017-18 regulators might want to limit access to those patients with genetic disease, and extend coverage more widely only when they can be shown to prevent cardiovascular events and deaths. While cost is not technically a consideration, it will be on the back of everybody's minds when deciding who is eligible for the PCSK9s.

Project	Praluent	Repatha
Company	Sanofi/Regeneron	Amgen
NPV	$5bn/$2.2bn	$7.9bn
% of market cap	4%/4%	6%
Event type	FDA advisory committee	FDA advisory committee
Date	June 9, 2015	June 10, 2015

PCSK9s have proven themselves more potent than statins like Crestor at lowering low-density lipoprotein cholesterol (LDL-C), the so-called "bad cholesterol" responsible for cardiovascular disease. As injectable antibodies they are expected to be significantly more expensive than statins, most of which have lost patent protection.

In getting Praluent and Repatha to market, Sanofi and Amgen have been tactical in proving that they lower cholesterol in limited populations like patients with familial hypercholesterolaemia. This is a population almost sure to get a green light, but the question will be how many additional patients will be encompassed by the label.

The FDA's announcement on the advisory committee raises the possibility that additional populations like the statin intolerant and patients who have not controlled their LDL-C with statins will also be permitted. The view of the outside experts is likely to be more essential than usual in helping the FDA make its decisions.

On the one hand, cardiologists who see high-risk patients unable to control their cholesterol with statins, or who cannot tolerate statins, could be eager to support relaxed wording on the label. On the other, they may be reluctant to do so until it can be shown – through the Odyssey Outcomes trial of Praluent and the Fourier trial of Repatha – whether the PCSK9s cholesterol-lowering power leads to reduced heart attacks, strokes, cardiovascular deaths and other events.

This question is especially relevant as payers and physicians alike know that not every patient who can take statins does so, or that every patient is taking the appropriate dose (*Payer demands threaten rosy PCSK9 forecasts, September 11, 2014*).

Keep it smaller

As with the new hepatitis C drugs, payers are expected to take a hard-line approach with the PCSK9s – which are expected to cost more than $8,000 a year.

With the hep C drugs Sovaldi and Harvoni insurers in most cases restricted coverage to patients with worsening fibrosis or cirrhosis. With the PCSK9s, they will want to ensure that statin intolerance has been shown with multiple treatment cycles, and that statin intolerance is proven at a maximal dosage.

Officially, the FDA does not take cost into consideration when making an approval decision. However, it will weigh heavily on the discussion of appropriate populations in the absence of firm outcomes data.

As for differentiation, there is little to be found. Both lower cholesterol by more than 60% compared with placebo, so an efficacy argument will be difficult to win. Praluent has shown a higher rate of ophthalmic events, although still numerically low, according to an analysis by the information services company AdverseEvents. This finding is not likely to stand in the way of a positive vote or approval, however.

Given that it is looking like launches will be more or less in tandem – Praluent has a PDUFA action date of July 24, Repatha August 27 – market share will probably be earned with marketing muscle and payer strategy rather than clear-cut differentiation.

The advisory committee vote and subsequent FDA decision will help clarify the denominator of that market share calculation. But even if regulators and the cardiovascular community want that number to be big, payers will work to keep it as small as possible.

Study	**Trial ID**
Odyssey Outcomes	NCT01663402
Fourier	NCT01764633

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