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A Look At Leqvio's Lacklustre Launch

Novartis Cholesterol Drug Sales Still Stuck

by Kevin Grogan

The Swiss major's CFO Harry Kirsch told *Scrip* that US cardiologists are slowly but surely getting to grips with the 'buy-and-bill' reimbursement model for Leqvio, while EU sales are not going to grow significantly until cardiovascular outcomes data read out in a few years' time.

While soaring sales of the heart failure drug Entresto continue to drive *Novartis AG*'s cardiovascular franchise, the same still cannot be said for its closely-watched cholesterol lowerer Leqvio, which is taking a long time to gain traction in the market.

The Swiss giant had hoped Leqvio (inclisiran), a small interfering RNA directed PCSK9 twice-a-year injection, would shake up the market, overcoming some of the hurdles that slowed the uptake of the original PCSK9 drugs launched in 2015, *Sanofi*/*Regeneron Pharmaceuticals, Inc.*'s Praluent (alirocumab) and *Amgen, Inc.*'s Repatha (evolocumab). It was approved in Europe back in December 2020 and got the green light in the US a year later for the treatment of adults with clinical atherosclerotic cardiovascular disease who have had an event, or patients with heterozygous familial hypercholesterolemia (HeFH) who require additional LDL-C lowering. (Also see "*It's Time For Novartis To Put Its Leqvio Launch Strategy To The Test*" - Scrip, 22 Dec, 2021.)

However, the launch has not been a raging success and Novartis's second quarter sales show that Leqvio only contributed $78m to the firm's coffers. That is up from $22m in the like, year-earlier period but just $14m more than the first quarter of this year.

Speaking to *Scrip* as Novartis reported a strong set of financials for the second quarter overall, up 7% to $13.62bn, chief financial officer Harry Kirsch said that Europe made up a bit less than half of Leqvio sales which was a reasonable performance given reimbursement barriers in the

continent. Payers in many EU countries are waiting for cardiovascular outcomes data from the ORION-4 study before making any decisions on reimbursement but that is not expected to read out before July 2026.

Kirsch acknowledged that Leqvio's progress in the UK was "still a bit slow." In September 2021, some 20 months after unveiling an alliance with NHS England to give at-risk patients speedy access to the drug, Novartis secured reimbursement for Leqvio as part of a multi-faceted agreement that included plans for a large-scale primary prevention clinical trial evaluating the injection in patients at very high risk of having their first cardiac event. (Also see "*All Systems Go For Novartis 'World-First' Leqvio Pact With England*" - Scrip, 1 Sep, 2021.)

However, the much-heralded world-first collaboration has hit the rocks of late. There was a moratorium in the NHS on all non-COVID related initiatives and in March, Novartis said it would not proceed with the aforementioned primary prevention trial called ORION-17 which would have involved up to 40,000 patients. Instead, it will focus on the VictORION-1-PREVENT trial, a different primary prevention study that is looking to enrol 14,000 patients across 42 countries, including the UK and the US. (Also see "*Novartis Leqvio Launch Lags As COVID-19 Hinders England Access Scheme*" - Scrip, 2 Feb, 2022.)

As for the US, Kirsch noted that the main hurdle to broader adoption of Leqvio continues to be resistance by cardiologists to establish the 'buy-and-bill' infrastructure needed to get reimbursement under Medicare Part B, or the medical benefit, rather than Medicare Part D, the pharmacy benefit. Novartis said that 54% of its "Leqvio source of business" in the US now comes through the buy-and-bill model, a system not generally used by cardiologists who must buy the drug upfront before administering it and being reimbursed, up from 18% in the first quarter.

Kirsch said that "we've seen steady progress but not yet the inflection" but reiterated Novartis's faith in the long-term prospects for Leqvio. He also pointed out the recent US label change earlier this month to cover patients with earlier stages of cardiovascular disease, which should help. The US Food and Drug Administration expanded approval on Leqvio for use in patients with high cholesterol who have an increased risk of heart disease, such as patients with hypertension or diabetes, as an adjunct to diet and statin therapy, and also removed four adverse reactions (urinary tract infection, diarrhea, pain in extremity and dyspnea). (Also

Buy-And-Bill A Bust For Novartis's Leqvio?

By Jessica Merrill

03 Jan 2023
The US commercial strategy for the PCSK9 inhibitor Leqvio was tied to reimbursement under Medicare Part B, but it hasn't developed the way Novartis envisioned.

Read the full article here

see "*Novartis Gets Expansion For Earlier Use Of Leqvio*" - Scrip, 11 Jul, 2023.)

Echoes Of Roche/Alnylam Pact

The access hurdles faced by Leqvio were further brought to mind this week by Roche linking up with *Alnylam Pharmaceuticals Inc.* to co-develop and co-commercialize zilebesiran, the RNA interference (RNAi) specialist's hypertension treatment which, like Leqvio, is also being developed to replace daily oral dosing with a twice-yearly injection. (Also see "*Eyebrows Raised As Roche Inks Cardiovascular Pact With Alnylam*" - Scrip, 24 Jul, 2023.)

Interestingly, part of the Roche/Alnylam link-up will see the two firms test the subcutaneously administered RNAi therapeutic, which targets angiotensinogen, in a cardiovascular outcomes trial prior to regulatory submission of zilebesiran. Having that data at launch suggests Roche has learned a lesson from Leqvio which should maximize the drug's commercial potential in a large, chronic disease.

Clearly, all is not lost for Leqvio and Novartis has regularly claimed that the launch could mirror that of the heart failure drug Entresto (sacubitril/valsartan), which also got off to a very slow start. Now it is the company's biggest earner - first-quarter sales shot up 35% to $1.52bn. (Also see "*Novartis Bets On Buybacks Due To Limited M&A Options*" - Scrip, 18 Jul, 2023.)