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Can Slow Selling Heart Drug Entresto Perk Up In 2017? Novartis Hopes So

By Sten Stovall

SALES OF NOVARTIS' ENTRESTO HAVE BEEN painfully slow and missed their 2016 target of $200m – but the big pharma hopes the heart failure drug's sales momentum will take off next year and it remains confident the first-in-class therapy will eventually reach peak annual sales of around $5bn.

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Entresto is **Novartis AG**'s key pipeline growth driver, but has had very slow uptake commercially, falling far below early expectations thanks to US market access barriers by payers. Novartis is now confident those hurdles are starting to melt away, prompting the diversified Swiss group to predict that prescription sales of the first-in-class ARNI therapy will triple over the coming year, as the group's sales force is now fully in place and reimbursement coverage in the US is more comprehensive.

Entresto, which combines the neprilysin inhibitor sacubitril with the angiotensin receptor blocker valsartan, accumulated full-year sales of $170m, below the company's initial target of $200m. But the company during its fourth-quarter and full-year presentation Jan. 25 forecast sales of the therapy, which won FDA approval in July 2015, will triple by fourth-quarter 2017, to at least $500m. Initial uptake of the drug has been much lower than expected due to reimbursement delays and challenges over its high yearly cost.

But Novartis used its full-year update to say US access has improved for all channels for the heart failure therapy - particularly for the key Medicare population where access has hitherto been most difficult. In light of that trend, the Swiss group during a four-hour investor presentation reiterated that it is confident the heart failure drug will gradually reach peak annual sales of around $5bn.

There have been previous attempts to jump-start the therapy's commercial prospects. In late 2016 Novartis tried to boost sentiment by releasing data supporting Entresto in preventing costly hospitalizations.

In November at the annual American Heart Association meeting it presented robust outcomes data in the PARADIGM-HF study, in which it slashed the rate of death or hospitalization for heart failure – the primary endpoint – by 20% compared with the generic angiotensin converting enzyme inhibitor enalapril, in heart failure with reduced injection fraction. But despite positive cost-effectiveness analyses, the drug has struggled to get off the ground commercially.

Datamonitor Sees Eventual Entresto Jump

Still, with Entresto now included on Medicare Part D and a number of major commercial formularies, Informa's Datamonitor Healthcare expects US sales to significantly increase over the coming years. Entresto has also received the strongest class I recommendation in both the US and European chronic heart failure treatment guidelines, which Datamonitor Healthcare believes will further enhance uptake of the drug in the chronic heart failure (CHF) indication. The new guidelines recommend Entresto as first-line treatment for CHF patients with reduced ejection fraction (HFrEF), with the drug expected to replace the ACE inhibitor Vasotec (enalapril; Merck & Co/Valeant) as the current standard of care. *(Also see "Outlook For Heart Failure Drugs Entresto And Corlanor Finally Looking Up" - Pink*

Sheet, 23 May, 2016.) Also, Novartis has enrolled Entresto in a large clinical trials program, FortiHFy, which is likely to provide additional data to support future label expansions to wider CHF patient populations.

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"Everything we're seeing on Entresto is giving us confidence in the future for the drug," Novartis CEO Joe Jimenez told reporters.

"For example prior authorizations are coming down in terms of requirements, and so the access hurdles that were put up are coming down very quickly. And our field sales force that we initiated mid-year in 2016 is now up and running and is highly productive. People have been trained and are in place. And we're starting to see a depth of prescription among our biggest targets of cardiologists increase," Jimenez said, adding: "The early warning indicators on this brand make us very bullish and we expect to triple scripts by the end of 2017."

Others Remain Skeptical On Entresto Surge

But that forecast uptick in prescription sales for Entresto was underwhelming for some observers.

"Clearly, there has been some negotiation on price to achieve this," commented Jefferies analyst Jeffery Holford, who added in a note that "all things considered, we see the below consensus target of $500m set for 2017 as a relatively low bar, though this makes sense given that 2016 revenue guidance was not met."

Roger Longman, CEO of Real Endpoints, an analytics company, said Novartis will need to navigate

numerous barriers to get better Medicare uptake and broader usage by cardiologists, who are loathe to switch heart patients on to different drugs if their current ones are still working. Administrative paperwork is another disincentive, he added.

He noted that Medicare Part D plans don't pay for hospitalization, so the outcomes data showing fewer people end up in hospital when using Entresto is a moot point. That must be viewed in light of the fact standalone prescription drug plans are only offered by private companies - like Humana - that have a contract with Medicare to administer them. Each plan provides coverage for a specific drug list, called a formulary.

"The most important thing about PDP plans is that they only cover drugs. So if you have a drug that reduces hospitalization which Entresto does, you as the administrator of the plan get no benefit – no offset – so you are paying for a much more expensive drug than those you funded before – which are essentially generic," Longman told *Scrip*. "Whereas if you were the owner of a Medicare Advantage Plan you could take a chance that the drug can reduce your medical expenses and offset the additional costs of the drug. But most of the people who would be prescribed Entresto are in these PDP plans. And that was one huge problem for Novartis."

Full-Year Update Underwhelmed Analysts

Novartis made its optimistic projections on Entresto during its fourth-quarter results update which coincided with an R&D-focused analyst meeting spanning several hours and which was, analysts said, a clear attempt to reassure investors that the group's pipeline – which it says has 13 potential blockbusters - can support longer-term growth and offset heavy losses due to the loss of patent exclusivity. Novartis is trying desperately to offset the loss of blockbuster drug *Gleevec* (imatinib) and faces fresh losses when *Gilenya* (fingolimod) goes generic in 2019, followed by *Afinitor* (everolimus) in 2020. This will be further aggravated by the patent loss by the end of the decade on two of the most important legacy **GlaxoSmithKline PLC** oncology drugs, the kinase inhibitor *Votrient* (pazopanib) and *Promacta* (eltrombopag), that the Swiss group recently acquired via their asset swap.

But analysts were skeptical of Novartis' ability to offset such losses.

Berenberg analyst Alistair Campbell noted that "with two or three more big generic hits just a few years away, it will have to execute extremely well in R&D to navigate that."

Alcon Review Result by End-2017

The firm also announced that the future of the group's troubled eye unit Alcon's is under review, with an IPO and or spin-off being considered as options. "All options are on the table", CEO Jimenez told reporters, and he didn't preclude a trade sale. The review of Alcon's operations will take place over the course of 2017, but any decision will apply only to the devices portion of the business, including surgical devices and contact lenses, as ophthalmic drugs have been integrated into the broader pharma business, he said. Novartis has been mulling a possible sale or spin-off of the underperforming Alcon for some time.

Analysts said Novartis' full-year results were largely as expected. Core operating income in 2016 fell 2% measured at constant currency basis due to generic erosion and growth investments. Core EPS was therefore $4.75, a decline of 2% year-on-year measured at constant currency basis

Looking to 2017, the company forecast group core operating income in 2017 to be broadly in line with the prior year to a low single digit decline measured at a constant currency basis and that the impact of generic competition on sales is expected to be around $2.5bn for the full-year.

Berenberg's Campbell described the company's 2017 outlook as "challenging", adding that "sentiment has been weakening on Novartis and these results are unlikely to help."

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