

Serelaxin setback puts focus on Entresto



[Madeleine Armstrong](#)

The prospects for Novartis's heart failure franchise have taken a major blow with the phase III failure of serelaxin. Not only has the company lost a potential blockbuster, it is now even more reliant on Entresto, which has so far struggled to live up to expectations.

Serelaxin's sales, which had been forecast to hit \$1.1bn by 2022, according to *EvaluatePharma* sellside consensus, might be a drop in the ocean for a company the size of Novartis – but the asset had still been billed as the group's top pipeline prospect (see table below).

Relax don't do it

The project had previously shown promise in the smaller Relax-AHF trial – enough at least for Novartis to press on with the 6,500-patient Relax-AHF-2 study after initially being knocked back by the FDA ([Event – Novartis writing second act in heart failure](#), December 8, 2016).

That promise has now evaporated with the company's announcement that Relax-AHF-2 did not meet its primary endpoints of reducing cardiovascular death through day 180 or reduced worsening of heart failure through day five when added to standard therapy in patients with acute heart failure.

Novartis did not give more details, and although it said it would evaluate the next steps for the programme it is almost certain that serelaxin will not get the go-ahead outside its only approved jurisdiction, Russia, where it is marketed as Reasanz. The company's Swiss-listed shares fell 1.5% today.

Removing serelaxin – which had been forecast to be the number-two heart failure therapy by 2022 – illustrates just how underserved the heart failure market is.

Top five heart failure products by 2022 sales

| Product | Company | Status | 2022e sales (\$m) |
|------------|----------|------------------------|-------------------|
| Entresto | Novartis | Marketed | 4,356 |
| Reasanz | Novartis | Marketed (Russia only) | 1,110 |
| Corlanor | Amgen | Marketed | 309 |
| Vericiguat | Bayer | Phase III | 291 |
| Finerenone | Bayer | Phase III | 222 |

Source: *EvaluatePharma*.

As for the rest of the top five, the development of Bayer's finerenone in heart failure seems to have stalled, with the company recently telling *EP Vantage* that it had chosen to prioritise the less competitive indication of diabetic kidney disease ([Bayer looks beyond Xarelto and Eylea](#), February 22, 2017).

Even Entresto is set to have a hard time living up to expectations. Sales so far have been sluggish, and the product brought in just \$170m in 2016, missing *EvaluatePharma* sellside consensus of \$198m.

Novartis had hoped that success with serelaxin could help it build a portfolio in heart failure, one of its areas of focus, but any cross-selling opportunities now look to be out of reach.

What next for Novartis?

Things have not been going smoothly for Novartis in other areas either: the recent approval of Kisqali in breast cancer came with safety warnings and monitoring requirements that could make it an also-ran in the CDK4/6 inhibitor space behind Pfizer's Ibrance and Lilly's abemaciclib ([Kisqali battles Ibrance on safety and cost](#), March 14, 2017).

Kisqali is forecast to be Novartis's fifth-biggest product by 2022, but could soon see a downgrade, particularly if abemaciclib, which recently posted a win in phase III, comes through with expected safety benefits.

There are still high hopes though for CTL019, which is vying with Kite Pharma's KTE-C19 to become the first approved CAR-T therapy and should be filed in the US imminently.

Even so, Leerink analysts believe that the "only meaningful stock-moving event" for Novartis will be the spin-out of its Alcon eyecare division. This might be a slight exaggeration, but the pressure is undoubtedly on the company to do something sooner rather than later.

Novartis's top five pipeline projects by 2022 sales

| Project | Description | Indication | Status | 2022e sales (\$m) |
|----------------------|--------------------------------------|---------------------------------------|-----------|-------------------|
| CTL019 | CAR-T therapy | Acute lymphocytic leukaemia, lymphoma | Phase III | 917 |
| BAF312/ siponimod | S1P 1 & 5 receptor modulator | Multiple sclerosis | Phase III | 865 |
| Midostaurin | FMS-like tyrosine kinase 3 inhibitor | Acute myeloid leukaemia | Filed | 436 |
| AMG 334* | Anti- CGRP MAb | Migraine | Phase III | 367 |
| Arzerra S.C. | Anti-CD20 MAb | Multiple sclerosis | Phase III | 266 |

*Co-development with Amgen; Source: EvaluatePharma.

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