ACC preview: a veri important test for Merck and Bayer

Heart failure data must repay Bayer and Merck & Co for taking a chance on vericiguat, and a hit for Medtronic’s renal denervation system could erase the shame of its 2014 failure.

The annual meeting of the American College of Cardiology will be held in Chicago towards the end of March, and will see two presentations that represent major catalysts – one in pharma, and the other in medtech.

On Saturday March 28, delegates will get a look at the full dataset from the Victoria study of vericiguat, under development by Merck & Co and Bayer for heart failure. The trial was toplined in November, with the guanylate cyclase agonist reducing the risk of heart failure hospitalisation or cardiovascular death over placebo in patients with chronic heart failure with reduced ejection fraction.

All the patients in the study are also being treated with standard of care, which includes Novartis's Entresto, and the extent of the improvement on top of this will be critical. Evercore ISI analysts write that a 20% risk reduction will be considered meaningful. It is also possible that a lower CV benefit would be considered a success should vericiguat also markedly improve quality of life.

The project’s performance in phase II does not provide much of a benchmark for predicting its chances in phase III. For one thing the endpoint here was completely different – reduction in NT-proBNP levels, a surrogate for cardiac stress – and for another the trials failed. Vericiguat only made it to the next stage of development because Bayer felt there was enough of a dose response and Mace benefit.

A hit in another pivotal trial, Vitality, in the harder-to-treat heart failure population – those with preserved ejection fraction – would also boost the project. But Bernstein analysts are sceptical that this will hit, Entresto and several other projects having failed. Data from Vitality are also imminent, though it does not have a late-breaker slot at the ACC.

Heart failure is a tough market to launch in, thanks to conservative practice, cost pressures and the slow pace of guideline changes. At least vericiguat will be added on to the standard of care, a much easier prospect than replacing it.

Bernstein sees global sales of the product peaking in 2030 at around $1.5bn, with the partners getting half each, and assigns a 25% probability of success.
A perfect Spyral

A day later, results from the US pivotal trial of Medtronic’s renal denervation product Symplicity Spyral will be presented, and these will have to be highly positive to justify the group’s hefty investment in this once-moribund technology.

Data on the first 80 of around 170 patients in the Spyral HTN-Off Med study yielded a surprise hit back in 2017, revitalising interest in the technique (The corpse of renal denervation starts twitching, August 28, 2017). In 2018 Medtronic had said it would start a pivotal trial of the Spyral device.

In mid-2018, however, there was a shift in the plan: instead of a separate pivotal study being started, the Off-Med trial would be expanded and recast as registrational. Enrolment was upped to 433 patients, and the time cut-off for the primary efficacy endpoint – ambulatory 24-hour blood pressure change from baseline – was altered from three years to three months.

It is the full data from this study that will be presented at the ACC meeting. The interim cut revealed a sham-adjusted drop in ambulatory blood pressure of 5mmHg, and Medtronic has previously said it hoped to get at least as big a reduction when the full data came out.

Drug therapy is of course the initial treatment for patients with hypertension; renal denervation is only used in those who do not respond or cannot tolerate the various medications. This is still an enormous opportunity, though, with Medtronic putting the renal denervation market “somewhere in the neighbourhood of ... $5-15bn”, according to Stifel analysts.

Medtronic recently started a 50-patient pilot study, Dystal, testing a targeted procedural approach with fewer radiofrequency ablations. This could allow faster and more efficient procedures. The decision to start this study suggests that Medtronic is optimistic about the Off Med results, though investors might wonder whether the group is getting ahead of itself.