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Novo sows the seeds for a new heart failure approach

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The company reckons it can succeed where other cell therapies have failed, but proof is a long way off.

Despite the existence of various heart failure drugs there is no cure for the condition. Novo Nordisk hopes to change that with HS-001, a cell therapy it is developing alongside the Japanese company Heartseed and which recently went into first-in-human trials.

Cell therapies for heart failure have fallen short in the past, but Novo believes that this time it might just work. For one thing, Novo is using a different cell type to previous attempts, which Jacob Sten Petersen, vice-president of the group's cell therapy R&D, likens to a different drug class.

Mesoblast, for example, used mesenchymal precursor cells in its failed project Revascor, while HS-001 is made up of cardiomyocytes. "Mesenchymal stem cells are healer cells – at least that's the theory, but it hasn't really worked," he tells *Evaluate Vantage*. "We're trying to replace the lost cardiomyocytes and thereby rebuild the heart. They're two fundamentally different approaches."

Secondly, HS-001 comprises clusters of these cells that, he says, are less likely to be pumped away by the heart than individual cells.

Novo is reluctant to use the word "cure", although a spokesperson said the company believes cell therapy could "halt or reverse" disease progression in heart failure and other indications.

Slow and steady

Novo and Heartseed still have a long way to go to prove this is indeed the case. The recently begun, Heartseed-led Japanese phase 1/2 trial, called Lapis, will not finish for two to three years, depending on how quickly the target 10 patients can be enrolled and treated, Mr Petersen says.

This looks set to be a slow process, with patients being monitored for several weeks before the next subject can receive HS-001 – a precaution that Mr Petersen puts down to a lack of approved stem cell-based therapies. "I think everybody agrees it's better to be safe than sorry."

The groups believe that Lapis, which will test HS-001 dosed at two levels, 50 million and 150 million cells, could support Japanese conditional approval. The study is primarily evaluating safety at six months, but secondary endpoints include left ventricular ejection fraction and myocardial wall motion.

In the rest of the world, however, where Novo is responsible for development, it will be a much longer road to approval.

Minimally invasive plans

In Lapis, HS-001 is being injected directly into the heart during a planned coronary artery bypass graft procedure. Mr Petersen acknowledges this will limit the population eligible for therapy; to address this the company is also developing a catheter for minimally invasive delivery via a blood vessel in the patient's leg.

A Japanese trial of the catheter-based approach, which could involve higher doses, will start around the time that Lapis ends – and it is this delivery tech that Novo hopes eventually to take into its first global trial.

All this means Mr Petersen is reluctant to say when development outside Japan might start.

Novo's cell therapy rivals will likely be taking a similarly cautious line. Other companies developing induced pluripotent stem cell-derived cardiomyocytes include China's Help Therapeutics, which recently received clearance to start domestic trials of HiCM-188, the Bayer subsidiary Bluerock and Japan's Orizuru Therapeutics.

While HS-001 is a very early bet, Novo has later-stage prospects in its push to become a cardiovascular player, including ziltivekimab. The company recently revealed pivotal plans in heart failure with preserved ejection fraction for the Corvidia-originated anti-IL-6 antibody.

This story has been updated to include comments from Novo about cell therapy's curative potential.