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Cytokinetics aims to become the Vertex of cardiovascular disease

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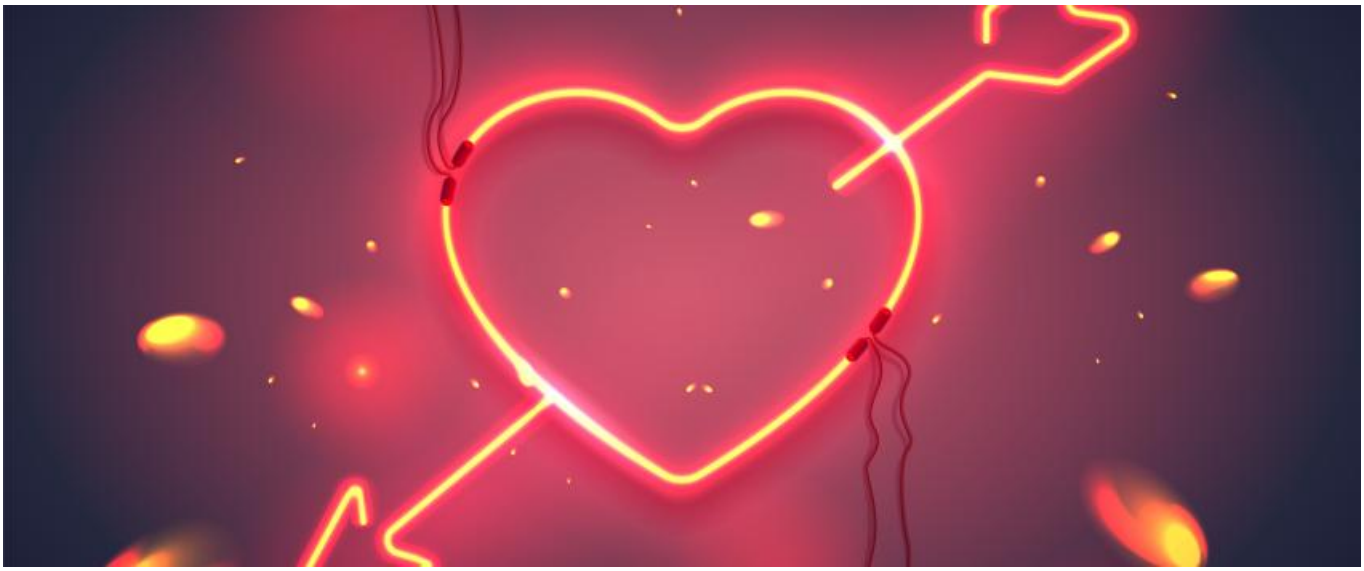

But a surprise adcom for omecamtiv mecarbil might put a spanner in the works.

Cytokinetics is not letting the small matter of losing a big biotech partner get it down. Amgen walked away from the heart failure project omecamtiv mecarbil in 2020, but the smaller group believes it has found a niche it can pursue alone, at least in the US – and it has even grander long-term plans.

Cytokinetics hopes to emulate the cystic fibrosis market leader Vertex, but in speciality cardiovascular indications, its chief executive, Robert Blum, tells *Evaluate Vantage*. Key to this goal will be getting approval for both omecamtiv and the company's next most-advanced asset, aficamten, currently in phase 3.

There are reasons to be cautious about the chances of omecamtiv, however, which is currently under review at the FDA with a Pdufa date of November 30. Last month, Cytokinetics disclosed that the FDA is planning an advisory committee meeting, catching some analysts and investors unawares.

Surprise!

"It was a surprise because they told us they weren't having it," Mr Blum says. "But they changed their mind."

He insists that nothing regarding the application has changed and there is "nothing that would suggest to me that there are any issues here. But I do think that pendulums swing and we may see more adcoms for new mechanisms of action."

As well as the novelty of omecamtiv, a myosin activator, a talking point will likely be how the asset performed in the subgroup of patients that Cytokinetics is homing in on; namely, those with severe heart failure, who drove the lacklustre hit in the pivotal Galactic-HF trial.

Specifically, omecamtiv seems to perform better in patients with the following characteristics at baseline: New York Heart Association class III or IV, left ventricular ejection fraction (LVEF) of 30% or less, and hospitalisation for heart failure within the previous six months. However, these data come from a post-hoc analysis, which could raise a red flag.

The FDA might choose to limit approval to the more severe end of the heart failure spectrum, but even if it does not these are likely the patients that would receive omecamtiv, Mr Blum concedes. However, he believes this is a big enough market for a company the size of Cytokinetics, estimating that this niche would encompass around one to two million of the total six million US heart failure patients.

But even here, omecamtiv could have a hard time going up against the likes of the SGLT2 inhibitors, which have shown strong results in heart failure. And, of course, there is the risk that the FDA could reject the project outright.

Next in line

The sellside is predicting omecamtiv sales of just $326m in 2028, according to consensus compiled by *Evaluate Pharma*. This helps explain why investors have largely shifted focus to Cytokinetics' next asset, aficamten, which is expected to become a blockbuster that year.

Not a myosin activator but an inhibitor, aficamten produced positive results in the phase 2 Redwood-HCM study in the rare disease hypertrophic cardiomyopathy (HCM), and Cytokinetics hopes to repeat this success in the pivotal Sequoia trial, which is currently enrolling patients with the obstructive form of the disorder.

Here, the group has a much bigger rival in the form of Bristol Myers Squibb, whose similarly acting drug Camzyos (mavacamten) got the nod from the FDA in April. Bristol gained the asset via its $13bn acquisition of Myokardia, which was originally a spin out of Cytokinetics.

Cytokinetics believes that aficamten could simplify therapy by avoiding the dose adjustments and interruptions that have been needed in Camzyos-treated patients whose LVEFs dropped too low.

Even if all goes well for Cytokinetics, the group could end up fighting an entrenched competitor for a piece of a small pie: only around 100,000 patients are currently diagnosed with HCM in the US.

This is thought to be an underestimate of the true numbers, though, and Cytokinetics could be a beneficiary of Bristol's education efforts, Mr Blum says. He believes that competition could be good all round, noting: "It tends to be this next-in-class compound that further expands the category, to the benefit of all participants."

He is reluctant to talk about aficamten's potential cost, but admits to being "surprised" at Camzyos's list price of nearly $90,000 per year – so it will be interesting so see whether Cytokinetics comes in lower, should aficamten make it to market.

The next Vertex?

The existence of aficamten should soften the blow if omecamtiv does get knocked back. But the latter's approval would allow Cytokinetics to put a sales team in place well ahead of any aficamten launch.

Mr Blum says the group has built a scientific franchise around myosin, and the next stage is to add a commercial force here, specifically to support a myosin activator and inhibitor. This strategy is backed by the fact that there is significant overlap between cardiologists who treat high-risk heart failure and those that treat obstructive HCM.

Accordingly, though myosin might seem like a speciality niche, if Cytokinetics can own it it could translate into a significant opportunity. Has any biotech pulled off anything similar in the past? "Vertex in cystic fibrosis," replies Mr Blum.

Now all Cytokinetics has to do is win over the FDA with omecamtiv and deliver a phase 3 hit with aficamten.