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Morphic looks to justify “oral Entyvio” excitement

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Big hopes have built behind Morphic’s MORF-057 in ulcerative colitis, and a key trial reads out imminently.

Morphic’s share price has enjoyed quite the run-up of late, climbing over 60% since the start of this year. The reason is growing investor enthusiasm about the group’s sole clinical asset, MORF-057, the results of whose Emerald-1 trial will likely be revealed during the second quarter.

Emerald-1 could position MORF-057, an oral alpha 4 beta 7 integrin inhibitor, as a real threat to Takeda’s marketed IV incumbent, Entyvio. Enthusiasm around MORF-057 first spiked back in 2021 when results of an early study were described by the company as spectacular. Still, those were just pharmacology data, and Emerald-1 will offer the first chance to see whether the project has clinical efficacy.

Integrin inhibitors are thought to work by suppressing excessive aggregation and invasion of inflammatory cells into the inflamed site of colonic mucosa in ulcerative colitis. They are playing for a sizeable market: Entyvio, launched in 2014, sold $5.5bn last year, a figure set to peak at $7.7bn in 2027, according to *Evaluate Pharma* sellside consensus.

Emerald-1 is a small, single-cohort phase 2 study, testing MORF-057 in just 40 ulcerative colitis patients. But its primary endpoint, change from baseline to week 12 in Robarts Histopathology Index (RHI) score, should offer a cross-trial comparison against Entyvio.

The Takeda drug is approved on the basis of clinical remissions versus placebo, but a phase 3 study, Varsity, reported a mean change from baseline in RHI of 7.5 points. Though this was at week 14 rather than 12 it does give a benchmark for Morphic to shoot for.

Morphic, having long positioned MORF-057 as an “oral Entyvio”, reckons its project can show a similar level of RHI improvement, and analysts generally agree that such a result in Emerald-1, with a clean safety profile, would constitute a win. Still, baseline characteristics will be important, as treatment-naive patients should do better than experienced ones.

Competition

MORF-057 is not the only non-IV challenger to Entyvio, but setbacks have blunted the competition somewhat, and each project’s target selectivity is slightly different.

Eisai/Kissei's Carogra was approved in Japan last May, but is apparently not in development in the US. Carogra, however, hits α4β1 as well as α4β7 integrins, and Roche has argued that action on the former integrin results in risk of progressive multifocal leukoencephalopathy, a serious side effect of the multiple sclerosis drug Tysabri.

To counter this the Swiss group was developing a SC contender, etrolizumab, which hit only the β7 subunit of α4β7 (as well as αEβ7) integrin, thus sparing α4β1. But Roche reported mixed data with etrolizumab in 2020, and later discontinued the project.

A SC form of Entyvio itself is approved in the EU, but received a US complete response letter in 2019; Takeda hopes for a positive FDA verdict this year.

The only other pure oral inhibitor of α4β7 integrin looks like Protagonist's PN-943. This too has put up mediocre data, in April 2022, but the company still hopes to find a partner.

It will be some time before MORF-057 has a chance to go before regulators. A presumably registrational, randomised, controlled phase 2 study, Emerald-2, was only initiated last November, and will not yield its first data until 2025.

And a final spanner in the works is Morphic's quiet $100m private placement on February 13. On the one hand companies not waiting until after a big clinical reveal to raise cash is often a negative sign; on the other some might hope that those who gave Morphic the cash might already have had a sneak preview of Emerald-1, which is after all an open-label trial.