Evaluate Vantage

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Protagonist seeks an Ideal readout

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A mid-stage hit with its ulcerative colitis project could see the company on course for blockbuster sales.

The departure of a senior executive just ahead of a major catalyst for their company might be regarded as a red flag. Whether this is an accurate interpretation in the case of Protagonist Therapeutics, whose chief financial officer, Don Kalkofen, stepped down on April 1, ought to become clear in the coming weeks.

Phase 2 data on the oral α4β7 integrin inhibitor PN-943 in ulcerative colitis are due in the second quarter. This project has been somewhat overshadowed by rusfertide's up-and-down fortunes, but a positive readout looks fairly likely – and the fact that Protagonist has already appointed a replacement for Mr Kalkofen could also be construed as a good sign.

Project	PN-943
Company	Protagonist Therapeutics
Market cap	$1.2bn
Product NPV	$1.2bn
% of market cap	102%
Event type	Ideal trial results
Indication	Ulcerative colitis
Date	Q2 2022

PN-943 is a second-generation analogue of PTG-100, an earlier molecule that was revived after a phase 2 study, initially thought a failure, was reinterpreted as a success. Success or not, Protagonist switched to the new molecule in late 2018, saying PN-943, which is also known as PN-10943, had better in vitro potency, target engagement and efficacy in disease models of colitis than PTG-100.

Data from the phase 2 Ideal trial will show whether the shift to the new agent was worthwhile. Two doses, 150mg and 450mg twice a day for three months, are being compared with placebo on their ability to cause remission in 150 patients with moderate to severe ulcerative colitis (UC).

Pill vs infusion

There is a major reason for investors to have faith in ’943: Takeda’s Entyvio.

This antibody, also an α4β7-specific integrin inhibitor, was approved for UC in the US in 2014 on the strength of the Gemini I trial, which showed a placebo-adjusted remission rate of 12% at six weeks and 26% at one year. This provides Protagonist a bar of sorts, though of course the timing of the endpoints and other aspects of the Gemini I and Ideal trials differ.

Protagonist’s previous candidate, PTG-100, mustered a placebo-adjusted remission rate of 11% at its highest dose. Theoretically the second-generation project, with its alleged higher potency and greater receptor occupancy, ought to beat this.

If it does, oral ’943 promises a convenience advantage over Entyvio, the market leader, which is infused at first and then given subcutaneously every two weeks. However, a small player like Protagonist will have a tough task going up against Takeda's marketing might.

Others are also vying to develop oral integrin inhibitors, including Morphic and Dice, although Protagonist is ahead of these rivals. Even if the group does succeed, though, the ulcerative colitis market is crowded, with another oral option, Abbvie's Jak inhibitor Rinvoq, recently getting the nod.

Leerink analysts suggest that a positive Ideal result could lead to a 50% rise in Protagonist’s shares, with a failure prompting a downturn of around 10%. Overall, they ascribe a 60% probability of success to PN-943 and project peak revenue of $1.2bn in 2030.

Crucially, Protagonist retains worldwide rights to PN-943: whatever happens when Ideal reads out, the company will own the result, at well as the molecule, outright.