Evaluate Vantage

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The other shoe drops for Gossamer's GB001

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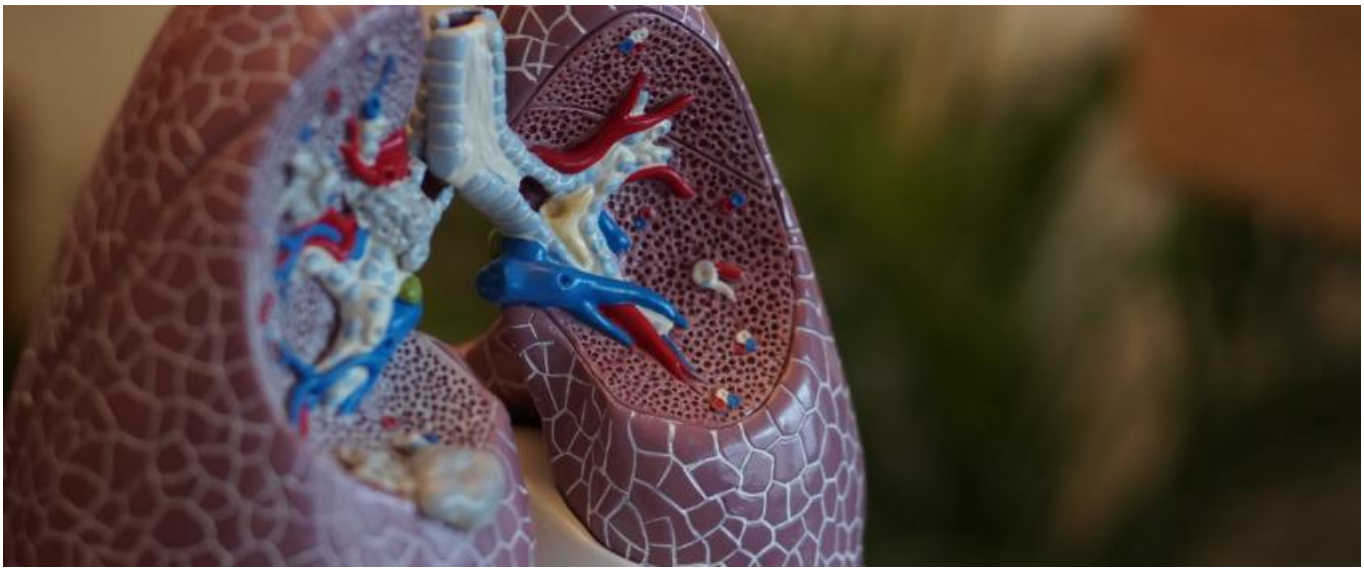

Novartis's similarly acting fevipiprant had failed in asthma in October, and today it fails in the more important severe setting.

Today's discontinuation of Novartis's fevipiprant blows a hole in the investment thesis behind Gossamer Bio. Like fevipiprant, Gossamer's lead asset, GB001, is a DP2 inhibitor targeting asthma.

At issue is fevipiprant's failure in the severe asthma setting of its Luster clinical programme, measuring exacerbations at one year. Until now Gossamer's argument had been that fevipiprant's October flop was irrelevant, as that had come in less sick patients. The markets had bought that excuse, causing the group's stock to nearly double since then, a surge that today looks foolhardy.

Fevipiprant is not the only proxy for GB001; *EvaluatePharma* reveals that a litany of other DP2 inhibitors have failed in asthma and been discontinued, including Array's ARRY-502, Boehringer's BI 671800, Novartis's earlier QAV680 and Astrazeneca's AZD1981. Coming into today Gossamer was capitalised at an incredible $1.5bn, but this morning the stock tanked 30%.

If at first

Fevipiprant's first setback had come in the pivotal Zeal 1 and 2 trials, which failed to meet their primary endpoints of FEV1 at 12 weeks in subjects with moderate asthma.

Today, Novartis said two remaining phase III studies in severe uncontrolled asthma, Luster 1 and 2, had also flopped. These had measured exacerbations at one year as a primary endpoint, and the failure was unequivocal: neither the 150mg nor 450mg fevipiprant dose worked, despite the data from both trials being pooled.

The Swiss group said this result "contributed to" its understanding of the DP2 pathway in asthma, but that it ultimately did not support fevipiprant's further development in this indication.

For Gossamer's GB001, which is expected to sell $272m in 2024, according to *EvaluatePharma* sellside consensus, this is bad news. The project's phase II Leda trial, in moderate to severe patients, is due to read out in in mid-2020, and an earlier study, while positive overall, failed to show a dose response.

If before fevipiprant's blow-up Gossamer bulls had argued that the Luster 1 and 2 studies would better indicate whether GB001 was a goer than Zeal 1 and 2, thanks to severe patients driving an expected benefit in Leda, today the rhetoric will have to change to remain current.

One difference, for instance, is that Gossamer is looking only at eosinophilic asthma, whereas the Luster trials had specified only that they would include subsets of subjects with “high eosinophil counts”. Gossamer’s primary endpoint is a composite including FEV1, rescue medication use and exacerbations, to indicate asthma worsening at 24 weeks.

Who else?

DP2, also known as CRTH2, is a prostaglandin receptor whose activation, developers argue, has been associated with allergy and inflammation.

Other clinical projects still in development targeting this pathway include Chiesi’s timapiprant (acquired along with Atopix), Pulmagen/Teijin’s PTR-36, and Idorsia’s ACT-774312, though the last is being studied not in asthma but in nasal polyposis.

Gossamer had pulled off a highly successful $276m Nasdaq flotation in February, and one reason investors stuck with the company in October is that it itself had indicated that the Zeal trials would likely fail. Today that credibility suffered a major sentiment knock-back, and Gossamer bulls and other DP2 inhibitor developers alike would do well to take note.