Evaluate Vantage

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Pfizer hands another asset to Roivant

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Does yesterday's deal with Roivant mean the pharma giant is cooling on TL1A targeting? And what about Prometheus?

The nascent TL1A-targeting space has emerged as one to watch this year, with both Pfizer and Prometheus talking up the potential of their respective antibody projects in inflammatory bowel diseases. This David and Goliath arrangement shifted yesterday with news that Pfizer was spinning out its lead asset.

Roivant has formed a new "Vant" subsidiary to take forward development of PF-06480605, now dubbed RVT-3101, and the obvious conclusion to draw here is that Pfizer has cooled on this mechanistic approach. The structure of the deal suggests that this is not necessarily the case, however, particularly as these two companies have been here before.

Priovant was created late last year to take Pfizer's Tyk2/Jak1 asset brepocitinib under what appear to be very similar terms. And Pfizer has had a commercialisation deal in place with Myovant since 2020.

The terms of this latest transaction see Pfizer retaining a 25% stake in the new Vant, which is fully responsible for funding the global development of RVT-3101. The Vant only owns commercial rights in the US and Japan. It also has an option to collaborate on a follow-on TL1A project currently in phase 1, which must be exercised before that asset moves into phase 2.

RVT-3101's clinical programme will be expensive: as well as inflammatory bowel diseases the project is to be tested in fibrotic conditions. This transaction takes costs off Pfizer's P&L, while allowing the pharma giant to retain a stake in the future.

It also allows Pfizer to focus investment on etrasimod, on which it spent $6.7bn; the ex-Arena asset is the star of Pfizer's extensive inflammation and immunology pipeline.

The big question

The Roivant-Pfizer history helps explain why Prometheus investors refused to be rattled by the development, with shares in the biotech slipping only 2.7% yesterday. The stock, which floated in March 2021, had come off highs in the last few weeks, possibly because investors anticipate a fundraising; the company is still worth a respectable $1.7bn.

Prometheus has always claimed that its TL1A candidate, PRA023, is the better MAb, with higher target engagement and a better immunogenicity profile than Pfizer's project. This remains to be proven, however, with crucial data on both of these mid-stage programmes imminent.

There is a strong biological rationale for pursing this approach. The TL1A protein belongs to the TNF superfamily; TL1A and its functional receptor DR3 is upregulated in colitis and the TL1A gene is thought to be convey susceptibility to inflammatory bowel diseases.

The bigger question is whether the mechanism can yield better responses than options already available. Answers should start emerging in the coming weeks.

Clinical-stage TL1A-targeting projects in inflammatory bowel disease		
Project	**Company**	**Trial details**
RVT-3101/PF-06480605	Roivant/Pfizer	Ph2b Tuscany-2 in UC, data due H1 2023; ph2 in CD completes Aug 2026
PRA023	Prometheus	Ph2 Artemis-UC (placebo-controlled) & Apollo-CD (single arm), data due Q4 2022; Athena-SSc-ILD completes Mar 2024
TEV-48574	Teva	Ph2 Relieve UCCD completes Aug 2024; ph2 in asthma previously terminated
Next-generation TL1A directed antibody	Roivant/Pfizer	In ph1 trials; Ph2 expected to start 2025.
Note: all are anti-TL1A MAbs. UC=ulcerative colitis; CD=Crohn's disease; SSc-ILD=systemic sclerosis-associated interstitial lung disease. Source: Evaluate Pharma & clinicaltrials.gov.		