Evaluate Vantage

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Prometheus takes on Pfizer in inflammatory bowel diseases

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It is make or break time for the smaller group's TL1A inhibitor PRA023.

When biotechs square up to big pharma it does not always end well for the minnows. But investors in Prometheus Biosciences clearly believe that this time it will be different, with the group seeing its stock climb steadily over the summer.

The optimism has been spurred by positive comments from Pfizer on its anti-TL1A antibody, PF-06480605 – Prometheus's lead project, PRA023, has the same mechanism of action. Data due soon could shed light on whether the smaller group has, as it hopes, the more effective agent.

The fourth quarter will see mid-stage results with PF-06480605 in ulcerative colitis, and PRA023 in both ulcerative colitis and Crohn's disease.

Projects	PF-06480605 & PRA023
Companies	Pfizer & Prometheus
Market caps	$259bn & $2.3bn
Product NPVs	N/A & $1.4bn
% of market cap	0% & 61%
Indications	Inflammatory bowel disease
Event type	Readout from ph2 Tuscany-2 (PF-06480605), Artemis-UC & Apollo-CD (PRA023)
Date	Q4 2022

PF-06480605 is expected to yield data first, from the phase 2b Tuscany-2 study. SVB analysts reckon these could come as soon as United European Gastroenterology Week on 8-11 October, while Wells Fargo suggests the American College of Gastroenterology meeting on 21-26 October as a potential venue.

Or Pfizer could drop the results during its next quarterly earnings call. PF-06480605 came to prominence during the group's third-quarter 2021 presentation, when the group highlighted a 34% endoscopic improvement rate in its single-arm phase 2a Tuscany-1 study in ulcerative colitis, comparing this with a 25% rate with the Jak inhibitor Xeljanz on a cross-trial basis. Endoscopic improvement was defined as a Mayo score of 1 or less.

Pfizer also disclosed a post-hoc analysis in which it found a 48% endoscopic improvement rate in biomarker-positive patients – without giving specifics about the biomarker used.

Since then, the big pharma has talked up PF-06480605. The company has had induction data from Tuscany-2 in house since the spring, and said earlier this year that these look consistent with those seen in Tuscany-1.

For Tuscany-2, Wells Fargo wrote that positive data would entail a 10% or higher delta versus placebo on clinical remission, and a 20%-plus difference on endoscopic improvement.

In July Pfizer started a phase 2 study of the asset in Crohn's, which was seen as another sign of confidence.

Prometheus on fire

All this has boosted Prometheus, which believes that PRA023 is the superior molecule, with higher target engagement and a better immunogenicity profile than PF-06480605.

This will be put to the test in the placebo-controlled Artemis-UC study in ulcerative colitis. Unlike Pfizer, Prometheus has prospectively defined its biomarker strategy, with its study comprising two cohorts: the first of all comers, and the second of TL1A-positive patients. It is the cohort one data that are due this year.

If PRA023 looks better than PF-06480605, this would be a big win for Prometheus. Wells Fargo believes that the best-case scenario would be a 15%-plus delta versus placebo on clinical remission, and a 25%-plus delta on endoscopic improvement.

In the single-arm Apollo-CD trial in Crohn's, the analysts hope for a 25% or greater rate of clinical remission and endoscopic response.

Pfizer and Prometheus were the only groups pursuing anti-TL1A antibodies for inflammatory bowel disease for some time. Recently they have been joined by Teva, which so far does not seem to be taking a biomarker-driven approach, SVB analysts noted.

Clinical-stage TL1A-targeting projects in inflammatory bowel disease

Project	Company	Description	Trial details
PF-06480605	Pfizer	Anti-TL1A MAb	Ph2b Tuscany-2 in UC, data due Q4 2022; ph2 in Crohn's completes Aug 2025
PRA023	Prometheus Biosciences	Anti-TL1A MAb	Ph2 Artemis-UC (placebo-controlled) & Apollo-CD (single arm), data due Q4 2022; Athena-SSc-ILD completes Mar 2024
TEV-48574	Teva	Anti-TL1A MAb	Ph2 Relieve UCCD completes Aug 2024; ph2 in asthma previously terminated

CD=Crohn's disease; SSc-ILD=systemic sclerosis-associated interstitial lung disease; UC=ulcerative colitis. Source: Evaluate Pharma & clinicaltrials.gov.