Evaluate Vantage

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Pressure piles up on pamrevlumab

Madeleine Armstrong

After the latest roxadustat clanger a phase 3 interim analysis in pancreatic cancer becomes even more important for Fibrogen.

On Monday Fibrogen snuck out a rather important disclosure on its first-quarter call: it has not been able to get its partner Astrazeneca to fund further trials of roxadustat in chronic kidney disease anaemia. True, development in myelodysplastic syndrome is ongoing, but the latest news will only fuel fears that Astra is about to walk away from the asset.

This development piles even more pressure on Fibrogen's wholly owned pipeline project pamrevlumab, which is facing a crucial moment soon. An interim analysis of the phase 3 Lapis trial will determine whether the company will be able to file for accelerated approval in pancreatic cancer.

However, in true Fibrogen style, it might be a while until things become clear. The company apparently does not expect to disclose the interim data, and instead plans to update investors "later in the year" after discussions with the FDA.

The news will disappoint anyone hoping that Fibrogen might become more transparent in light of the roxadustat controversy.

Project	Pamrevlumab
Company	Fibrogen
Market cap	$932m
Product NPV	$872m
% of market cap	94%
Event type	Interim analysis of event-free survival in ph3 Lapis trial
Indication	Locally advanced pancreatic cancer
Date	Q2 2022

Pamrevlumab inhibits connective tissue growth factor, which has been linked with both cancer and fibrotic

diseases. Lapis is testing the antibody plus chemo, versus chemo alone, in locally advanced unresectable pancreatic cancer.

The study has two co-primary endpoints: event-free survival, which will be the subject of the interim analysis, and overall survival. OS data are due in the first half of 2024; Fibrogen says that, whatever happens, the trial will continue to the OS analysis.

There are reasons to be cautious about whether Lapis will hit either of these endpoints. When reporting phase 1/2 pancreatic data, Fibrogen focused on the proportion of patients who became eligible for, and achieved, surgical resection.

The group did not give data on the more relevant measures of progression-free survival and OS, despite these being listed among that study's endpoints, as noted by the short seller Plainview in a 2019 report. As for overall response rate, pamrevlumab did not show a benefit versus chemo alone, according to a poster presented at Asco 2018.

After this story was published, *Evaluate Vantage* was made aware that full results from the study were later published in a paper.

If Lapis is unsuccessful, Fibrogen has a couple more shots on goal with pamrevlumab in Duchenne muscular dystrophy and idiopathic pulmonary fibrosis. The Lelantos-1 study in non-ambulatory DMD is due to yield data in the first half of 2023, while results from the Zephyrus-1 trial in IPF will follow mid-year.

The first half of 2023 will also see readout of the Matterhorn study of roxadustat in MDS. This could be Fibrogen's last chance to salvage something for that project, in the US at least.

Given Astra's apparent reluctance to commit more money in CKD anaemia, it is looking increasingly likely that Fibrogen will need to fund a new study itself if it wants to move forward there. Stifel analysts flagged "ex-US monetisation" of pamrevlumab as the only clear option for generating cash for this purpose.

Of course, this will depend on whether pamrevlumab actually works – something that might not become clear for some time.