Evaluate Vantage

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Abbvie flips Galapagos the bird, again

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Galapagos contemplates life without Abbvie as Pelican trial results disappoint.

Galapagos was already behind Vertex in the race to get a cystic fibrosis triplet to market, and now it might have fallen out of the running entirely. Unimpressive results from the Pelican trial have cooled the interest of its partner Abbvie, and Galapagos might soon need to choose between going it alone in cystic fibrosis or ditching the programme entirely.

Galapagos bulls probably do not see this problem, and will no doubt point to the fact that after losing Abbvie as a partner on filgotinib Galapagos signed up Gilead on much better terms. But this is a different case entirely: with Vertex so dominant in CF, Galapagos would need knock-out data to attract a new partner and, eventually, compete with the market leader.

Pelican flops

So far, Galapagos does not have this. The Pelican trial, of the company's C2 corrector GLPG2737 plus Vertex's approved CF drug Orkambi, did meet its primary endpoint, showing a significant reduction in sweat chloride versus Orkambi plus placebo at 28 days.

But this was lower than the sweat chloride reduction seen with Vertex's investigational CF triplets in phase II over a similar treatment period – although the usual caution about making cross-trial comparisons applies.

Cross-trial comparison of Galapagos and Vertex CF candidates

	Mean chg in sweat chloride vs baseline, mmol/l	Mean chg in ppFEV1 vs baseline
GLPG2737 + Orkambi (Pelican)	19.6	3.4%
Phase II trial of VX-659/tezacaftor/ivacaftor	42.2	9.7 percentage points
Phase II trial of VX-445/tezacaftor/ivacaftor	39.6	11 percentage points

Source: Company releases.

And GLPG2737 did not meet a key secondary functional outcome measure, change in FEV1 – falling short of Vertex’s triple combo projects, which have managed to show a significant benefit here.

The Pelican results raise the question of whether GLPG2737 adds much to Orkambi in the population studied, patients homozygous for the F508del mutation – and were clearly enough to give Abbvie cold feet. The bigger company took the opportunity to say it would not continue development of a separate in-house triple from Galapagos comprising GLPG2737, GLPG2222 and GLPG3067.

Given that Pelican was at least nominally positive Abbvie's doubts likely centre around Galapagos's lack of clinical relevance in the face of Vertex's dominance. Galapagos already has a fully owned triplet in phase I, made up of GLPG2737, GLPG2222, plus a different potentiator, GLPG2451; that is in the Falcon study, set to yield data in the third quarter.

As well as seemingly having the edge on efficacy, Vertex is well ahead of Galapagos in terms of development too, having already started phase III trials of its chosen triplets, VX-659/tezacaftor/ivacaftor and VX-445/tezacaftor/ivacaftor.

Falcon faltering?

After the Pelican disappointment, Galapagos therefore needs Falcon to impress – if it does not Abbvie could walk away from the partnership entirely.

Galapagos appears to be trying to dump Abbvie before it gets dumped, saying yesterday that it was “reviewing the future” of the collaboration with the bigger company.

But, if it does end up alone in CF, will it even be worth Galapagos’s while to continue? “Unless Falcon produces exceptional data it would make little sense to persist in CF, particularly given Vertex’s dominant position,” Stifel analysts wrote.

Galapagos has bigger fish to fry, including the Jak inhibitor filgotinib, now partnered with Gilead. Phase III data in rheumatoid arthritis, from the Finch 2 trial, are due in the third quarter, which could give an idea how filgotinib stacks up against other Jak inhibitors like Lilly’s Olumiant and Abbvie’s upadacitinib.

So far, the sellside has been cautious about the prospect of success for Galapagos’s CF pipeline – still, the company’s stock was down 6% today. While some optimistic Galapagos investors believe that Abbvie’s expected exit could leave the way clear for an even better deal, the market reaction suggests that a partner, however reluctant, is better than none at all.

Study	Details	Trial ID	Data?
Pelican	GLPG2737 + Orkambi in 22 F508del homozygous CF pts	NCT03474042	Reported
Falcon	GLPG2737 + GLPG2222 + GLPG2451 in 24 F508del homozygous & F508del/potentiator nonresponsive CF pts	NCT03540524	Q3 2018
Finch 2	Filgotinib in rheumatoid arthritis	NCT02873936	Q3 2018