Evaluate Vantage

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JP Morgan 2022 – Abbvie looks to crack the cystic fibrosis code

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Phase 2 data could indicate whether the big pharma has a chance of disrupting Vertex's monopoly.

When it comes to cystic fibrosis Vertex is the undisputed heavyweight, but this has not stopped other groups from taking it on. Abbvie is the latest challenger, and data due this quarter could give clues about whether the group was wise to go all in on projects originated by Galapagos.

Abbvie has two phase 2 trials under way, one of a doublet and one of a triplet. The big pharma reckons it can do better than Vertex's latest drug, the triplet Trikafta, in terms of efficacy – but an edge on tolerability could also be enough to justify moving forward, Abbvie execs hinted at the JP Morgan meeting this week.

Vertex is not standing still, and already has a next-generation triplet in phase 3; the Skyline 102 and Skyline 103 studies of VX-121, tezacaftor and VX-561 are set to complete next year. That group's chief executive, Reshma Kewalramani, talked up the high bar set by Trikafta, concluding that: "If it is possible to improve on Trikafta, we're determined to be the ones who do so."

Project	CF doublet (ABBV-3067 + ABBV-2222); CF triplet (ABBV-3067 + ABBV-2222 + ABBV-119)
Company	Abbvie
Event type	Phase 2 data
Indication	Cystic fibrosis
Date	Q1 2022
Trial IDs	NCT03969888 (doublet); NCT04853368 (triplet)

Trikafta is a triplet comprising elexacaftor and tezacaftor, both CFTR correctors, plus ivacaftor, a potentiator. It was approved in 2019 for patients homozygous for the F508del mutation in the CFTR gene, and those with one copy of the F508del mutation and one minimal function mutation (known as F508del/Min) – thereby addressing 90% of the cystic fibrosis population (*Vertex's double cystic fibrosis surprise, October 22, 2019*).

Trikafta is forecast to be the biggest cystic fibrosis drug in 2026 with sales of $9bn, according to sellside

consensus compiled by *Evaluate Pharma*.

No wonder Abbvie wants a piece of the action. The group has a triplet in development combining two correctors – ABBV-2222 (galicaftor) and ABBV-119 – with the potentiator ABBV-3067 (navocaftor). It is also evaluating a doublet comprising ABBV-2222 and ABBV-3067.

This quarter, the group is due to report topline data and make a decision on whether to take the programme forward, Abbvie's president, Michael Severino, said. When asked what the group would need to see versus Trikafta, he replied: "Our goal would be to be better from an efficacy perspective."

Abbvie believes that a marginal improvement could be enough, with execs previously saying the group was striving for an efficacy advantage of just a few percentage points on forced expiratory volume in 1 second (FEV1). But this would be on a cross-trial basis: Abbvie's studies are comparing its assets versus placebo.

The table below shows what Abbvie is up against, both in F508del homozygous and F508del/Min patients. Abbvie's doublet study is in homozygous patients only, while the triplet is being evaluated in both F508del homozygous and heterozygous subjects.

Going up against Trikafta: what Abbvie will need to show		
Population	**F508del/Min**	**F508del homozygous**
Trial ID	NCT03525444	NCT03525548
Change in ppFEV1	13.8*	10.0**
Change in sweat chloride	41.2*	45.1**
*All efficacy figures given at 4 weeks. *Relative to placebo; **relative to Smydeko (tezacaftor plus ivacaftor). Source: Trikafta label.*		

However, efficacy is not the only consideration, according to Mr Severino: "There could be advantages, for example, on drug interactions or tolerability. We'll look at that entire package."

Trikafta's label carries warnings about liver injury and cataracts.

Still, improved tolerability might not count for much if Abbvie's triplet cannot at least equal Trikafta on efficacy.

Mix 'n' match

Despite Abbvie's bullishness about ABBV-2222, which it has described as a "best-in-class corrector", the group's progress in cystic fibrosis has been far from smooth. In 2018 it discontinued development of a triplet comprising ABBV-2222 and ABBV-3067 – then known as GLPG2222 and GLPG3067 – plus a different corrector, GLPG2737.

And yet another combo, GLPG2222 plus GLPG2451 and GLPG2737, disappointed in the Falcon trial. Despite this, Abbvie opted to take over the cystic fibrosis programme from its partner, Galapagos (*Abbvie's low-risk bet could challenge Vertex on price, October 25, 2018*).

That deal spurred hopes of cost competition in cystic fibrosis, where Vertex's monopoly has meant it has had the freedom to set high prices. But first, Abbvie needs to convince on efficacy.