Evaluate Vantage

November 18, 2021

Arcus’s near dream scenario

Jacob Plieth

Gilead opts in at long last, and that’s more than many might have been expecting.

Given that in today’s biotech market deals that fall short of a full-blown takeover sometimes disappoint, Gilead today opting in to several Arcus pipeline assets might be seen as falling short of a dream scenario. In reality, however, this is a better outcome than level-headed Arcus investors had a right to expect.

Most had focused on the anti-Tigit MAb domvanalimab, and the glaring fact that no meaningful data had been disclosed for it, with Arcus instead issuing a mealy mouthed statement that seemed to kick the opt-in can down the road. But in fact Gilead has opted to license in not only domvanalimab but three other key assets too, giving Arcus a $750m windfall.

Domvanalimab was a particular focus because the Tigit mechanism has generated a huge amount of interest, courtesy largely of Roche’s tiragolumab. And under Gilead’s 2020 tie-up with Arcus domvanalimab was singled out as the most lucrative programme, capable of triggering a $275m opt-in payment plus up to $500m in regulatory milestones.

However, keenly awaited data disclosure, thought to be key to determining whether Gilead opted in, did not materialise. In June Arcus merely said the Arc-7 study had met “internal thresholds”, and then 10 days ago – still revealing no data – it stated cryptically that Gilead had “initiated its opt-in review process for our anti-Tigit programme”.

Surprise!

Thus today’s news that Gilead was picking up not only Tigit but also etrumadenant and quemliclustat should come as a pleasant surprise, and the multiple projects involved increased the opt-in fee to $725m. Arcus traded up 15% this morning.

Etrumadenant is an adenosine A2a/A2b receptor antagonist, while quemliclustat is a small-molecule CD73 inhibitor. The opt-in also includes a second Arcus anti-Tigit MAb, AB308, while the original tie-up had given Gilead rights to zimberelimab, the anti-PD-1 MAb with which domvanalimab is being combined in the Arc-7 trial.

Domvanalimab is Fc-silenced, an approach Arcus had argued was a key differentiating factor, though there was little scientific data to back such a claim. Most other Tigits have functioning Fc regions, though a notable exception here is Compugen’s COM902.

However, Arcus’s recent advancement into the clinic of AB308, an Fc-active project, was seen by some as

suggesting a lack of faith in domvanalimab, and consequently as a sign that the Arc-7 data were too weak to persuade Gilead to sign on the dotted line. Gilead actually opting in to both assets takes all such speculation off the table.

On triggering the opt-in today small changes were made to the 2020 tie-up, slightly reducing ex-US royalties payable by Gilead and cancelling a $100m option continuation payment Arcus had been due to receive next year. Gilead retains rights to opt in to additional Arcus's clinical projects at $150m a pop.

Arcus bulls will note that the opt-in does not rule out an eventual takeover, though this surely now becomes a distant catalyst. And, with the entire clinical pipeline now in Gilead's hands, along with a 19.7% equity stake, the chances of any other company making an approach must be close to zero.

Beholden to Gilead: selected Arcus pipeline assets

Project	Mechanism	Selected trial	Gilead involvement
Zimberelimab	Anti-PD-1 MAb	Arc-7, ph2 1st-line NSCLC, domvanalimab combo +/- etrumadenant	Licensed under 2020 deal
Domvanalimab	Anti-Tigit MAb (Fc-silent)	Arc-10, ph3 1st-line PD-L1 ≥50% NSCLC, zimberelimab combo	Licensed under 2021 opt-in
Etrumadenant	Small-mol A2a/A2b receptor antagonist	Arc-6, ph2 in prostate cancer, various combos	Licensed under 2021 opt-in
Quemliclustat (AB680)	Small-mol CD73 inhibitor	Arc-8, ph2 1st-line pancreatic ductal adenocarcinoma, zimberelimab + chemo combo	Licensed under 2021 opt-in
AB308	Anti-Tigit MAb (Fc-active)	Arc-12, ph1 zimberelimab combo in various cancers	Licensed under 2021 opt-in
Unnamed	Anti-CD39 MAb	Preclinical (Wuxi tie-up, competes with Surface's SRF617 & Astrazeneca/Innate Pharma's IPH5201)	None
AB521	HIF-2α inhibitor	Preclinical (competes with Merck & Co's Welireg & Arrowhead's ARO-HIF2)	None

Source: company presentations & Evaluate Pharma.