Evaluate Vantage

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ISTH 2021 – Blackstone's Novartis spin-out scores

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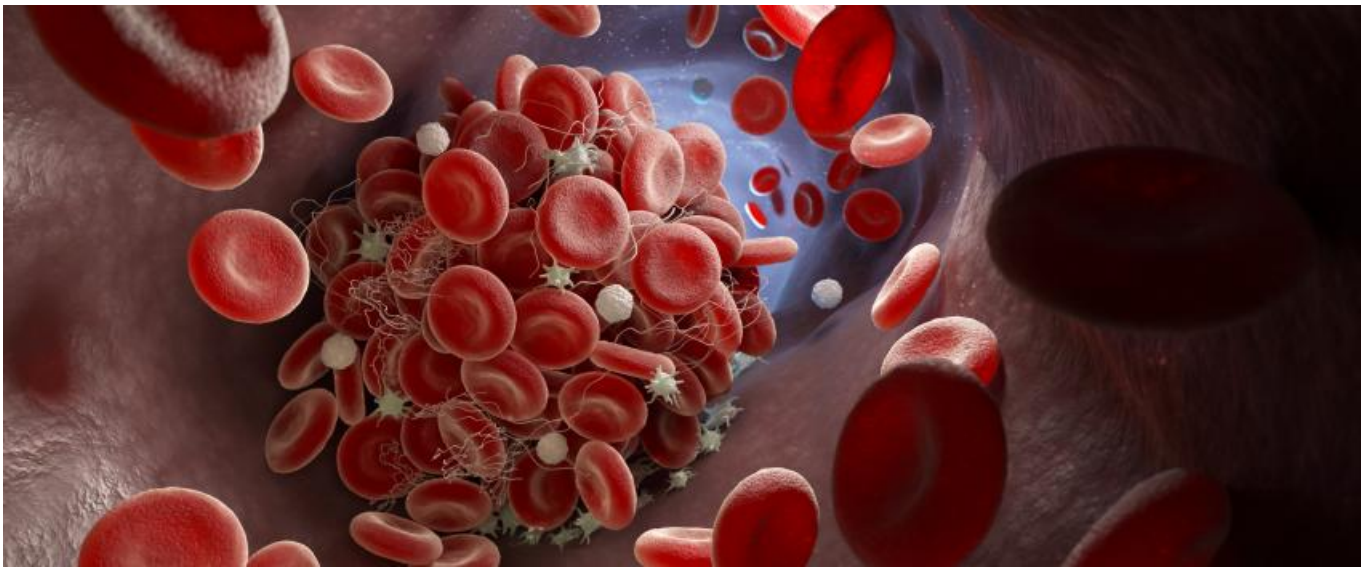

Abelacimab justifies its spin-out into the Blackstone-backed private biotech Anthos Therapeutics, and a big deal could follow.

An unusual factor XI inhibitor Novartis had given up on might have a shot at approval after all. Abelacimab, now in development by the private company Anthos Therapeutics, has shown the utility of this mechanism by scoring in a mid-stage trial in preventing venous thromboembolism.

The highest two of three doses of the project beat the anticoagulant enoxaparin in the trial, just presented at the ISTH meeting and published in the NEJM, while the lowest demonstrated non-inferiority. There will be celebration over this result at Blackstone Life Sciences, which in 2019 had taken a $250m punt in setting up Anthos as a spin-out from Novartis to focus on the development of abelacimab.

Anthos is still a one-project company, whose mission is to realise the goal of factor XI inhibition, which it calls the holy grail of haemostasis-sparing anticoagulation. Under its 2019 founding Novartis retained a minority equity stake, but the $250m start-up cash came from Blackstone and funds managed by the venture capital firm.

The fact that abelacimab is a project targeting a large cardiovascular use makes it a typical big pharma asset, setting up the prospects of deal making for the next stage of its development. The molecule actually derives from a 2004 discovery alliance between the Swiss firm and Morphosys, and was initially coded MAA868.

In 2018 Novartis had registered two phase 2 studies on clinicaltrials.gov, testing abelacimab in total knee replacement and atrial fibrillation, but both were cancelled before recruiting their first patient.

Clinical trials of abelacimab (MAA868)			
Study	**Indication**	**Sponsor**	**Status/result**
NCT03398434	Atrial fibrillation	Novartis	Withdrawn
NCT03393481	Total knee replacement	Novartis	Withdrawn
NCT04213807	Atrial fibrillation (dose-ranging, vs placebo)	Anthos	Completed
AZALEA-TIMI 71	Atrial fibrillation (vs Xarelto)	Anthos	Enrolling 1,200 subjects
ANT-005	Total knee arthroplasty (vs enoxaparin)	Anthos	Superior at two highest doses, non-inferior at lowest
Source: US & EU trial registries.			

Anthos's success came in a separate study of 412 subjects undergoing elective total knee arthroplasty that compared 30mg, 75mg and 150mg postoperative abelacimab doses against enoxaparin, a generic low-molecular weight heparin frequently given postoperatively to reduce VTE risk.

The primary efficacy endpoint was development of venous thromboembolism, which was seen in 13%, 5% and 4% of patients on the respective three active doses, versus 22% for enoxaparin. The two highest doses showed superiority to enoxaparin, with $p<0.001$, and the neat dose-response relationship will be seen as a nice bonus in what is, after all, a relatively small trial.

A key red flag with any anticoagulant is bleeding risk, and "clinically relevant nonmajor bleeding" occurred in 0-2% of subjects dosed with abelacimab, representing what the researchers termed a "low risk", and none in those on enoxaparin. Clearly a much larger study will be needed to tell definitively if targeting FXI can "dissociate thrombosis from haemostasis", the paper concludes.

For now, however, Anthos and Blackstone will celebrate the fact that abelacimab appears to have delivered what it had promised to: an antithrombotic profile that fits into the unmet need presented by the fact that all approved anticoagulants interfere with haemostasis, and thus increase bleeding risk.

Competition?

Abelacimab is a MAb that binds to the catalytic domain of factor XI, trapping it in an inactive conformation and neutralising the enzyme before it enters the coagulation process. *Evaluate Pharma* reveals Bayer's osocimab as another anti-FXI MAb in clinical development.

However, the paper's authors point out that osocimab failed to beat enoxaparin postoperatively, and was superior only when given preoperatively. Bayer and Ionis have also studied an antisense FXI project, IONIS-FXI-LRx, in phase 1.

Oral inhibitors of the related factor XIa are in development at Bristol Myers Squibb (BMS-986209), Ono (ONO-7684), Bristol/J&J (milvexian) and Bayer (asundexian).

As this is a big pharma area it would be logical for Anthos to license phase 3 development and commercialisation rights to player with a large primary care sales force. Perhaps Novartis will be interested in getting back into a project it had originated – after all, it has form, buying back Speedel in 2008 to regain its blood pressure drug Tekturna.

Alternatively, an Anthos IPO might maximise private investors' gains. Either way, Blackstone's bet looks like it might pay dividends just two years after being made.