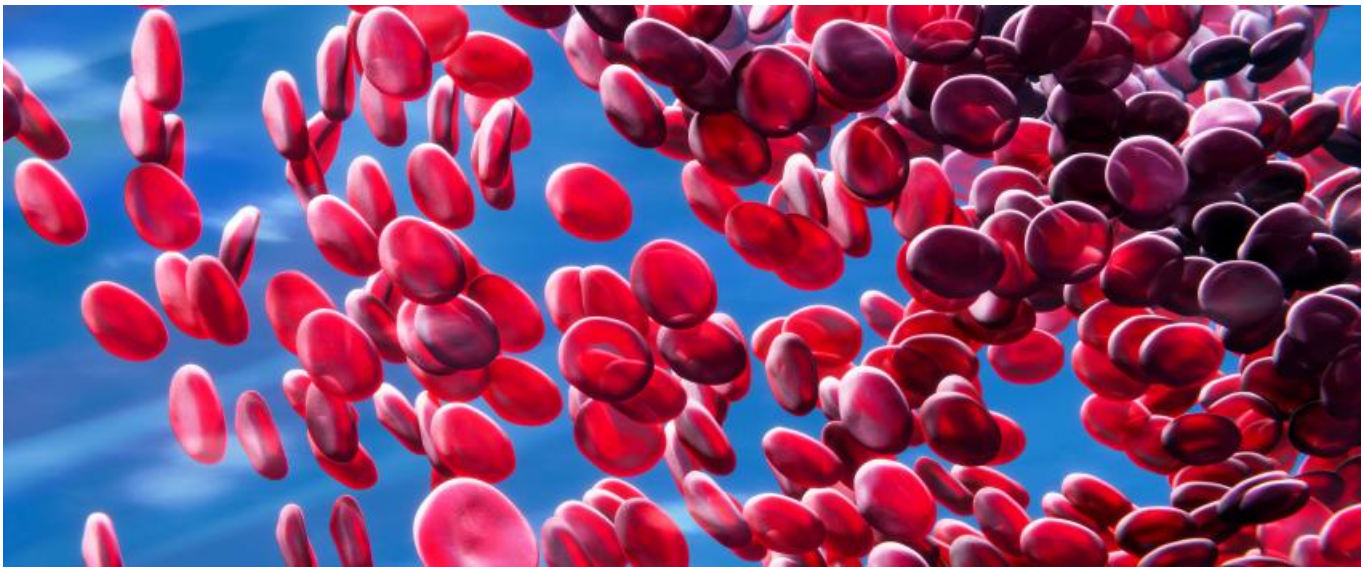
Evaluate Vantage

February 22, 2021

Biocryst looks to raise the profile of its factor D inhibitor

Jacob Plieth



The relatively low-key asset might at least partly be responsible for Biocryst shares more than doubling since the start of December.

Biocryst stock is up 120% since the start of December, and the group's oral factor D inhibitor BCX9930 might be one reason why. The sellside has previously not paid this pipeline asset much attention, but with clinical data due within weeks this might change.

One sign of BCX9930's growing prominence is a royalty financing deal Biocryst did two months ago, part of which was specifically earmarked for BCX9930's development for complement-mediated diseases like paroxysmal nocturnal haemoglobinuria (PNH). Still, the expected phase I PNH data are very early, so perhaps investors should curb their enthusiasm for a while.

The financing deal, done with Royalty Pharma, concerned Biocryst's just-approved hereditary angioedema drug Orladeyo. In return for royalties on Orladeyo and BCX9930 Royalty Pharma gave Biocryst $125m in cash, and a separate loan of up to $200m was arranged with Athyrium Capital Management.

The combined $325m was, Biocryst said, to be used to support the Orladeyo launch and development of BCX9930, as well as paying off an earlier credit facility with Midcap Financial.

Competitive

BCX9930 plays in a competitive field: Alexion boasts two factor D inhibitors, danicopan, in phase III, and ALXN2050, both derived from Achillion, and when Alexion's takeover is completed these will be in Astrazeneca's hands.

Factor D acts on the so-called alternative complement pathway, upstream of C5, and inhibiting it has the advantage of oral dosing. But C5 inhibition comprises two intravenous Alexion/Astrazeneca juggernauts, Soliris and Ultomiris. And another branch of the alternative pathway features Novartis's oral factor B inhibitor iptacopan in phase III.

So what is now expected from BCX9930's phase I trial? The study enrols treatment-naive PNH patients as well as inadequate responders to standard of care Soliris or Ultomiris. Evercore ISI analysts expect data in up to 16 subjects, comprising both groups.

Early data showed three of four treatment-naive subjects responding, with haemoglobin levels rising above

11g/dl. Because haemoglobin is lost when red blood cells break apart in PNH, its reduced levels are a direct indicator of disease severity.

Clearly a continuation of this sign of efficacy, with decent tolerability, is needed in additional naive patients to maintain the momentum.

Even more important will be initial results in pretreated patients, where the project is given on top of C5 blockade. This will be closely watched for cross-trial comparison against danicopan and iptacopan, which have been studied in similar settings.

Alternative complement pathway blockade in PNH patients inadequately controlled on Soliris or Ultomiris			
	Iptacopan	**Danicopan**	**BCX9930**
Company	Novartis	Alexion/Astrazeneca	Biocryst
Mechanism	factor B inhibitor	factor D inhibitor	factor D inhibitor
Study*	NCT03439839	NCT03472885	NCT04330534
Number of patients	10	11	Around 4
Baseline haemoglobin	not given	mean 7.9g/dl	TBC
Increase from baseline	mean 2.9g/dl	mean 2.4g/dl	TBC
End of study haemoglobin	>12g/dl in 8 of 10**	mean 10.3g/dl***	TBC
*Note: *all given in combination with Soliris; **at week 13; ***at week 24. Source: company presentations.*			

And Evercore points to another key dataset, namely findings in patients who respond poorly to standard of care, who after the initial combination period have Soliris withdrawn. However, these results are unlikely to be mature enough to be revealed at the next update, and are more likely to come later in the year.

Either way, with still undemanding sales forecasts of $78m in 2026, according to *EvaluatePharma* consensus, BCX9930 offers the sellside opportunities to upgrade the stock.

And it provides a handy distraction from Biocryst's misfire in coronavirus: two weeks after the royalty financing deal the group's antiviral galidesivir showed no clinical efficacy versus placebo in Covid-19.