Evaluate Vantage

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BioCryst hit with a HAE-maker

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BioCryst Pharmaceuticals' efforts in hereditary angioedema (HAE) so far look no more promising than previous attempts in gout and hepatitis C. Today the group's lead agent, avoralstat, bombed in a phase III prophylaxis trial, with two doses failing to show even a numerical benefit versus placebo.

As has been the case with BioCryst in the past, company executives had another pipeline project to which they could pivot, a phase I HAE asset called BCRX7353, not to mention another formulation of avoralstat that has shown better bioavailability in animal tests. Investors were not impressed, however, with shares plummeting 67% to $2.01 in early trading.

HAE that's not good enough

BioCryst's spin was that the liquid-filled soft gel formulation simply did not deliver enough active ingredient to have an effect on the frequency of HAE attacks – colloquially, "we didn't put enough gas in the tank", BioCryst said. The trial found that patients taking 500mg a day had an attack rate of 0.63 per week, on 300mg had a rate of 0.71, and those on placebo recorded 0.61.

The knock-on effect has been a delay in initiating phase II trials for BCRX7353 until the end of the year, as executives said they now wanted to make sure they design a trial that maximises the pill's chance of success. In any case, BioCryst is sitting on a $100m cash pile, which it says will be sufficient to fund it through important data for '7353, as well as a solid-tablet formulation of avoralstat.

Current timelines suggest that these candidates, if successful in the clinic, would be ready for regulatory submission in 2019. However, BioCryst only plans on progressing with the better of the two candidates once efficacy and safety data are a little clearer.

As analysts had pencilled in this formulation of avoralstat for a 2018 launch, it was not surprising that investors were displeased with news that the HAE pipeline would not generate revenue until 2020 at the earliest. *EvaluatePharma*'s consensus had been forecasting avoralstat sales in 2020 of $233m, a number that will now be deleted from all of their models.

Is it special?

BioCryst has been working on inhibiting kallikrein, an enzyme that triggers the inflammatory peptide bradykinin that is overproduced in acute HAE episodes. The leading agents in this condition – with a prevalence of one in 10,000-50,000 – are either inhibitors of bradykinin, in the case of Shire's acute treatment Firazyr, or, in the case of Shire's prophylactic treatment Cinryze, increase levels of circulating C1 esterase, which inactivates kallikrein.

Among avoralstat's unique selling propositions has been oral delivery, kallikrein inhibition and prophylactic treatment. Since the 2014 launch of Cinryze, which Shire acquired with its takeout of ViroPharma, a preventative treatment has been on the market.

Meanwhile, DX-2930, or lanadelumab, looks like it could be a kallikrein inhibitor on the market as early as 2017 – and, ominously, this is also in Shire's hands thanks to its takeout of Dyax (*It's not Baxalta, but Dyax will do nicely for Shire, November 2, 2015*).

This leaves oral delivery as the BioCryst pipeline's sole advantage. Should either the new avoralstat or '7353 come good, BioCryst could be in a tough fight with Shire over a tiny market.

Study	Trial ID
Opus-2	NCT02303626

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