Evaluate Vantage

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Sanofi scores a win with long-acting haemophilia project

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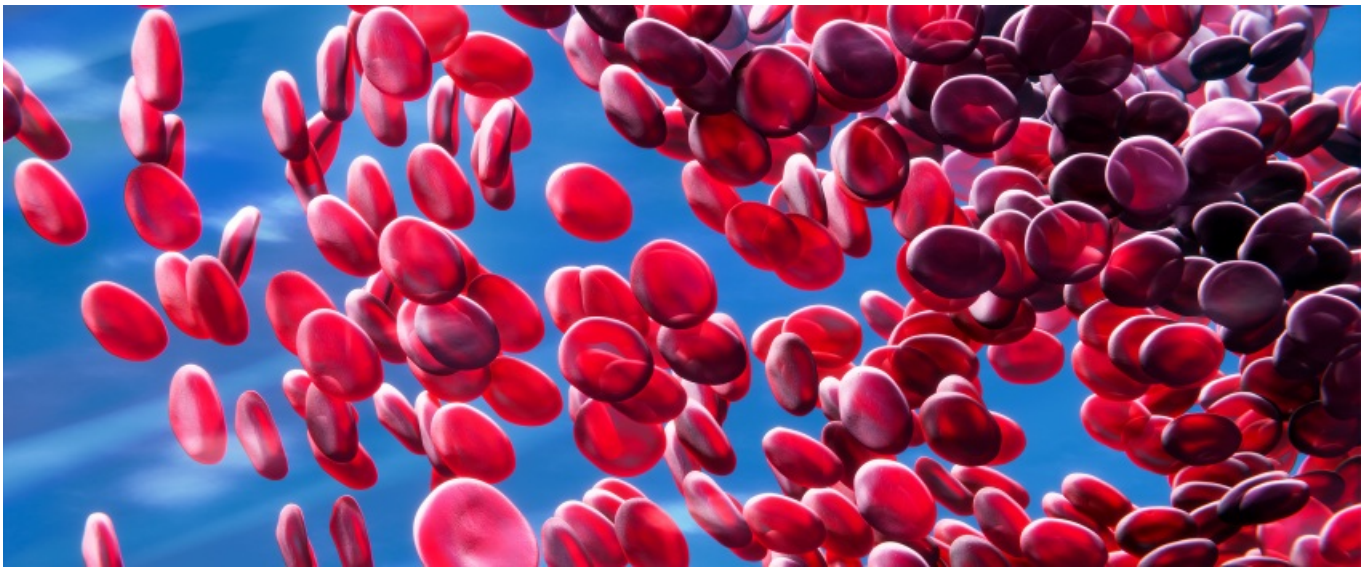

Interim results on bleeds look impressive, but more data are needed to gauge efanesoctocog alfa's chances against Roche's Hemlibra.

A few years ago haemophilia gene therapies looked like the death knell for traditional factor replacement. But Sanofi's faith in factors appears to have paid off, with promising interim pivotal data released today on its ultra-long-acting FVIII therapy, efanesoctocog alfa.

True, there is not much to go on, but annualised bleeding rates look at least as good as those seen with Biomarin's haemophilia A gene therapy contender, valoctocogene roxaparvovec (valrox), and better than with the market leader, Roche's Hemlibra. Efanesoctocog alfa is given intravenously just once a week, making it more convenient than existing FVIII products.

But Hemlibra is a subcutaneous once-weekly therapy, and has also been deemed cost-effective by the US pricing watchdog Icer – albeit in the context of even more expensive FVIII prophylaxis. Sanofi might need compete on price if it is to unseat its established rival.

As for other haemophilia A hopefuls, a new option could be bad news for gene therapy developers, which are already facing questions about lack of durability and appetite for such treatments. One view is that, in diseases for which therapies already exist – like haemophilia A – the risk/reward equation might not be strong enough for regulators or patients.

Normal range?

Sanofi and its partner Sobi will soon be taking efanesoctocog alfa, which was previously known as BIVV001, to regulators, and the latter company's stock climbed 6% today.

But there are still some gaps to fill in from the phase 3 Xtend 1 study. For one, the companies have not yet released any data on patients' FVIII levels – an important, albeit surrogate, endpoint.

Investors will hope that the pivotal trial can replicate phase 1/2 findings of 51% FVIII activity at day four and 17% at day seven. 51% is in the normal range, and 17% is "still quite strong protection even at the end of the week", as Sanofi execs put it during the group's fourth-quarter earnings call.

During that call, Sanofi's chief executive, Paul Hudson, raised the possibility that efanesoctocog alfa could be dosed even less frequently than once weekly. Existing extended half-life FVIII products are given twice a week.

Though once-weekly, Hemlibra has a black box warning for thrombotic events, and Sanofi has previously suggested that efanesoctocog alfa could have an edge on safety. However, today's release did not say much about adverse events, except that no patients receiving efanesoctocog alfa developed inhibitors, and that the most common treatment-emergent events were headache, arthralgia, falls and back pain.

Low bleeding

On bleeding rates, meanwhile, efanesoctocog alfa's benefit seems pretty emphatic.

Xtend-1 enrolled 159 haemophilia A patients without inhibitors who had previously received treatment with a FVIII product or Hemlibra. It had two cohorts: in arm A patients received 50IU/kg of prophylactic efanesoctocog alfa once weekly for a year; in arm B they got efanesoctocog alfa on demand for six months, then weekly prophylaxis for another six.

The primary endpoint was the annualised bleeding rate in arm A. The mean ABR was 0.71, which looks in line with results recently reported for valrox – and better than that seen in the non-inhibitor study of Hemlibra. The usual caveats about cross-trial comparisons apply.

Sanofi gained efanesoctocog alfa through the $11.6bn takeout of Bioverativ in 2018, along with some marketed products. The pharma group will no doubt want to recoup some of these costs, but if its new project does get to market Sanofi will need to pull off a delicate balancing act on pricing if it wants to be a real contender.

Cross-trial comparison of annualised bleeding rates with haemophilia A therapies

Project	Company/ies	Study	ABR
Efanesoctocog alfa (BIVV001)	Sanofi/Sobi	Xtend-1	0.7
Valoctocogene roxaparvovec (valrox)	Biomarin	Gener8-1	0.9*
Hemlibra	Roche	Haven-3	1.5**

**Data at one year in "rollover population"; **once-weekly dose, treated bleeds. Source: company releases & product labels.*