Evaluate Vantage

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Upcoming events – Pfizer and Glycomimetics await sickle cell data and Biocryst tries again

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Rivipansel needs to help sickle cell patients leave hospital sooner and BCX7353 faces established hereditary angioedema agents.

Welcome to your weekly digest of approaching regulatory and clinical readouts. Bluebird Bio might have figured out a way to cure sickle cell disease, but the price and inconvenience of its gene therapy Lentiglobin means there should be space for therapies for less severe patients. Glycomimetics and Pfizer are locked in a battle with Novartis and, separately, Global Blood Therapeutics to launch treatments to relieve the symptoms of the blood disorder.

The Glycomimetics/Pfizer candidate, rivipansel, is due phase III results by the end of the second quarter in patients hospitalised with vaso-occlusive crises, the painful episodes resulting from blood vessel blockages caused by sickle-shaped red blood cells. A pan-selectin antagonist, rivipansel is designed to reduce the cell adhesion, activation and inflammation that is believed to reduce blood flow.

Patients in the Reset trial were randomised to rivipansel or placebo. Those in the active treatment arm were given an intravenous dose of 1,680mg of rivipansel initially, followed by subsequent 840mg doses every 12 hours – patients weighing less than 40kg received a weight-based dose. The primary endpoint is readiness for discharge, which is expected to be an average of five days after admission.

In a phase II trial, patients taking rivipansel plus standard of care treatments did not achieve readiness for discharge significantly faster than patients on standard of care alone. However, that was a secondary endpoint, with the primary outcome measure – also missed – being time to resolution of the vaso-occlusive crisis. In addition, that trial was smaller, enrolling 76 patients compared with the 350 in Reset.

Pfizer has assumed control of clinical development in phase III. Glycomimetics is due up to $80m based on development milestones, so a positive outcome would be welcomed by the smaller group, which is in the midst of independently funding phase III development of its E-selectin inhibitor uproleselan.

Rivipansel is forecast to achieve $104m in sales in 2024, earning $34m in royalties for Glycomimetics, according to *EvaluatePharma*'s consensus of sellside analysts.

Meanwhile, Global Blood Therapeutics and Novartis are approaching sickle cell patients from slightly different angles. GBT's voxelotor (GBT440) aims to increase haemoglobin, while Novartis's crizanlizumab (SEG101) selectively blocks P-selectin to arrest the vaso-occlusive process. While neither one would directly compete

with rivipansel for hospitalised patients, if they are successful in preventing crises they could reduce the number of patients needing hospital treatment.

Another try at HAE

North Carolina-based Biocryst Pharmaceuticals has been good at picking itself up after failure, leaning heavily on its investors as it has done so. This resilience has brought the company to the verge of reporting pivotal data for its next oral hereditary angioedema (HAE) project, BCX7353, in the second quarter.

The kallikrein inhibitor is being tested as a preventive treatment, and at a minimum will need to better Biocryst's first HAE candidate avoralstat, which failed to significantly reduce the rate of HAE attacks when compared with placebo and was subsequently discontinued (*BioCryst hit with a HAE-maker, February 8, 2016*).

BCX7353 will probably also need to stack up well against the other preventive HAE agents, Takeda's Takhyzro and Cinryze, and CSL's Haegarda. Similar efficacy might be enough for Biocryst's oral agent, which promises greater convenience over Cinryze, which is given intravenously, and Takhyzro and Haegarda, which are delivered via subcutaneous injection.

The Apex-2 trial of BCX7353 has enrolled 96 patients and will measure the number of HAE attacks over 24 weeks with BCX7353 dosed at 110mg or 150mg, and placebo. Takhyzro's 26-week trial has set the bar: patients treated with a dose of 300mg every two weeks experienced a significant 87% reduction in the number of attacks per month versus the placebo group.

However, BCRX7353's chances look shaky after mixed results in the phase II Apex-1 trial. The study tested doses of 62.5mg to 350mg, and only one of these, 125mg, hit significance, reducing the number of HAE attacks by 74%.

Success would be very welcome for Biocryst investors, who have been tapped for $195m since March 2017. The company's backers have also seen two mergers fall apart, with Presidio and Idera, although both of these turned out to be bullets dodged (*Idera's reinvention takes a hit, December 17, 2018*).

Most recently, Biocryst expanded its debt facility with Midcap Financial Trust, adding $20m to an existing $30m vehicle. Another $30m will be available if Apex-2 reads out successfully enough to merit a new drug application, and an additional $20m if the US FDA approves BCX7353.

The project is forecast to achieve $149m in sales in 2024, according to *EvaluatePharma*'s consensus of sellside analysts, which will be a welcome addition to the meagre $9m in sales expected for Biocryst's marketed influenza antiviral Rapivab.

If BCX7353 fails, Biocryst has an asset or two waiting in the wings, with its oral factor D inhibitor BCX9930 and the antiviral galidesivir having entered phase I. However, the company's executives should not expect many of the existing investors to stick around if Biocryst needs to make this pivot.

Trial	ID
Reset	NCT02187003
Apex-2	NCT03485911