Evaluate Vantage

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Agios gets a pre-Ash boost

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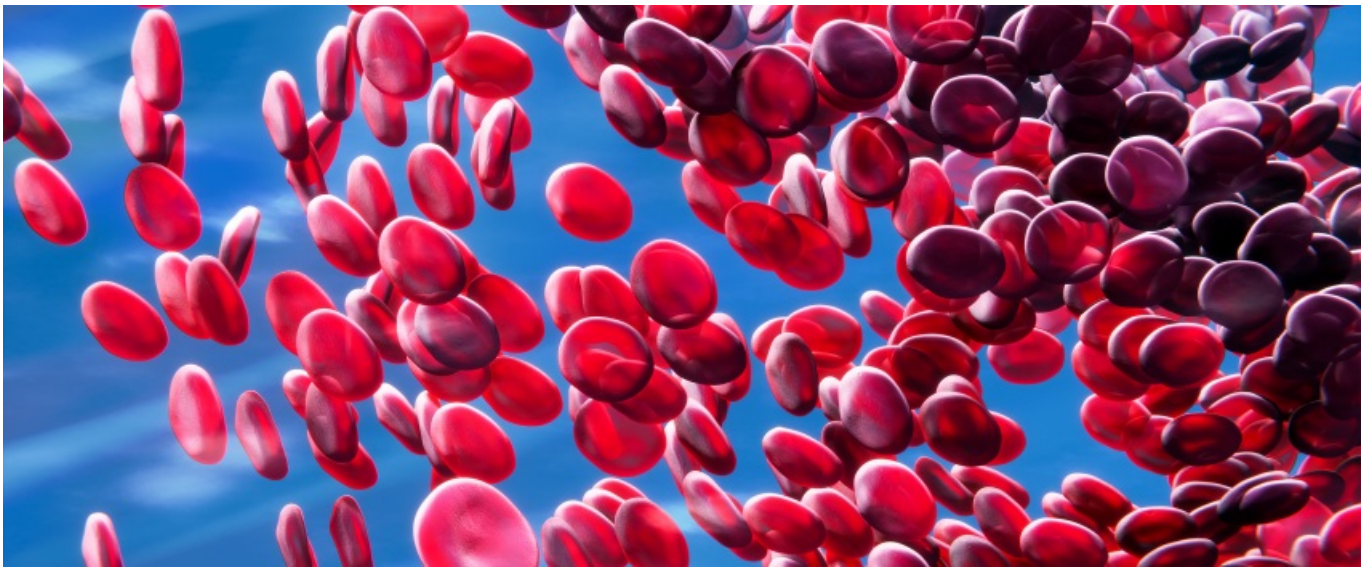

Mitapivat's pivotal win in a rare type of anaemia could bode well for its chances in thalassaemia and sickle cell disease.

Agios Pharmaceuticals will soon be heading to regulators after its lead pipeline project mitapivat scored in its first phase III study, in the rare anaemia pyruvate kinase deficiency.

The pivotal win also provides important validation of the pyruvate kinase R activator, which is being trialled in the much bigger indications thalassaemia and sickle cell disease. Agios's stock opened up 4% this morning after the group reported that 40% of mitapivat-treated patients in the Activate study in PKD achieved a haemoglobin response, versus none in the placebo arm ($p<0.0001$).

The company said the trial, in patients not receiving regular blood transfusions, also hit key secondary endpoints including average change from baseline in haemoglobin. Agios hopes to present full data at the European Hematology Association meeting next June.

One focus will be safety: toxicity worries with mitapivat have previously caused jitters, with a vaso-occlusive crisis in an early sickle cell disease trial deemed possibly related to the project. That study also found three cases of heart rate increases, although the company has stressed that these were asymptomatic and that cardiac events have not been seen in other studies of mitapivat.

All Agios is saying for now is that mitapivat's safety profile in Activate was "generally consistent" with previous data.

All in all, the data look in line with results from the phase II Drive PK study, which found that 50% patients achieved a haemoglobin response. And the definition of a responder in Drive PK study was slightly more lenient.

Agios has another pivotal readout on the horizon. The Activate-T trial, in more severely affected PKD patients who regularly receive blood transfusions, is set to yield top-line data in the first quarter of next year.

Ash is coming

On the nearer-term horizon are further data from a phase I sickle cell trial: results from eight patients were presented at this year's EHA meeting, and data on around 11 patients are expected on Monday at the American Society of Hematology congress.

Ash will also feature data on Forma Therapeutics' rival pyruvate kinase R activator FT-4202 in sickle cell

disease.

Sickle cell would be the most lucrative prize for these agents, but the pipeline is getting crowded. Meanwhile, there are currently no approved therapies for PKD, according to Agios.

Mitapivat is forecast to bring in $591m in 2026, according to *EvaluatePharma* sellside consensus. Leerink analysts, meanwhile, put peak sales at $1.7bn, with $1.1bn of this coming in sickle cell, $364m in thalassaemias and $290m in PKD.

Clinical trials of Agios's mitapivat				
Setting	**Status**	**Trial name**	**Trial ID**	**Note**
Pyruvate kinase deficiency (non-transfusion dependent)	Phase 3	Activate	NCT03548220	Met primary endpoint*
Pyruvate kinase deficiency (transfusion dependent)	Phase 3	Activate-T	NCT03559699	Top-line data due Q1 2021
Alpha/beta-thalassaemia (non-transfusion dependent)	Phase 2	AG348-C-010	NCT03692052	Interim data reported at EHA 2020; ph3 to start 2021
Sickle cell disease	Phase 1 (NIH-led)	N/A	NCT04000165	Interim data reported at EHA 2020 (8 pts); more due at Ash 2020 (~11pts)

**Haemoglobin response, defined as ≥1.5g/dl increase from baseline sustained at 2 or more assessments at weeks 16, 20 & 24 during the fixed-dose period. Sources: EvaluatePharma, clinicaltrials.gov, company presentation.*