Evaluate Vantage

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Ash 2020 preview – late-breaker puts Uniqure in pole position

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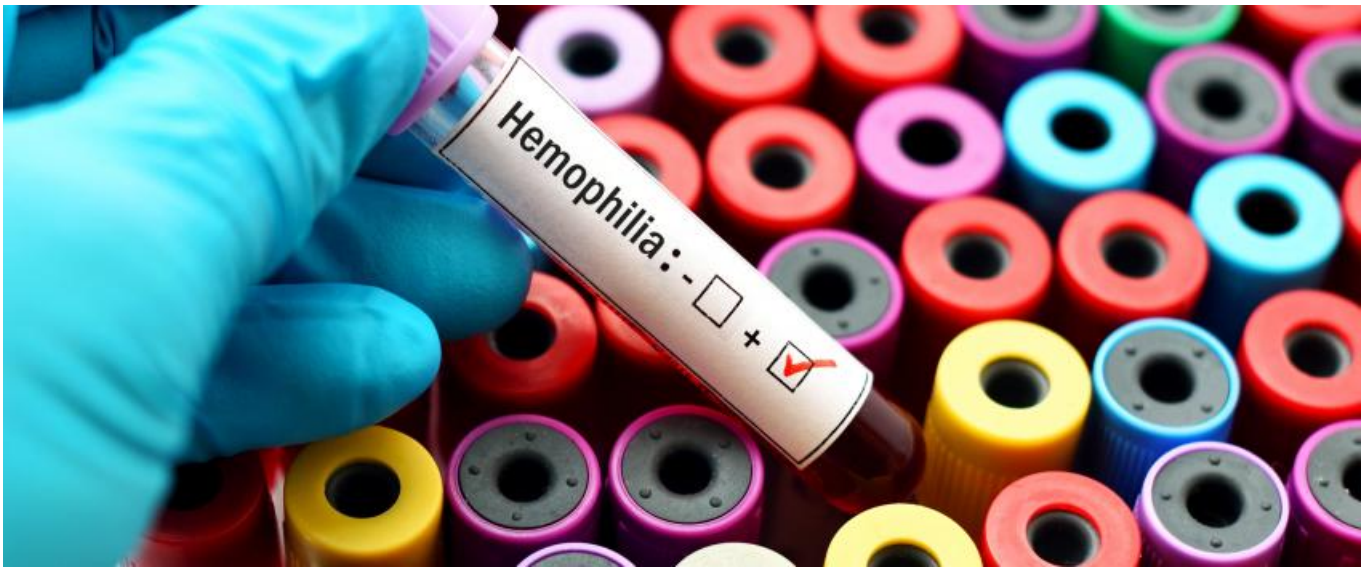

Among the upcoming haematology meeting's non-oncology presentations Uniqure's haemophilia B gene therapy scores a valuable late-breaker.

With results of Uniqure's pivotal Hope-B study securing a place among the Ash meeting's six late-breaking abstracts, unveiled yesterday, the company will be working hard to maintain its claim that etranacogene dezaparvovec is the best-in-class gene therapy for haemophilia B.

The results look reasonably robust, and with efficacy broadly in line with phase II data Uniqure stock put on 8% yesterday. Still, there will be questions about one patient who did not respond, and investors will look for additional detail on durability and bleed episodes when the findings are presented in full at the conference in two weeks.

First results

The abstract shows the first results from the phase III Hope-B trial, a 54-patient single-arm study of etranacogene dezaparvovec (AMT-061). Uniqure switched to this Padua variant factor IX gene therapy when it became apparent that its older project, AMT-060, based on a wild-type FIX variant, was not efficacious enough.

Hope-B has shown mean factor IX activity of 37% of normal at 26 weeks – in line with the activity seen in Uniqure's phase II trial (*Uniqure turns the screw on Spark and Pfizer, February 8, 2019*).

In addition, 72% of patients were bleed-free during the 26-week period. 15 subjects experienced 21 bleeds, and Evercore ISI analysts said more information was needed on these; it is not clear if there is room for improvement here as even normal people bleed under certain circumstances.

Interestingly, 23 of the 54 patients had pre-existing AAV5 antibodies, which would have excluded them from studies of rival gene therapies, such as Pfizer/Spark's fidanacogene elaparvovec.

In Hope-B the presence of these antibodies did not appear to affect the efficacy of etranacogene in patients with antibody levels titres up to 678.2, which Uniqure says encompasses over 95% of the general population.

However, a question remains over patients with very high antibody levels. One, with a neutralising antibody titre of 3,212.3, did not respond. There was an infusion reaction in another patient, and this subject got only a partial etranacogene dose.

As with all gene therapies, durability will be important. Uniqure says that, after talking with regulators, it plans to incorporate FIX activity and bleeding rates at 52 weeks as co-primary endpoints.

Selected non-oncology presentations at Ash 2020			
Project	**Company**	**Detail**	**Abstract**
Etranacogene dezaparvovec	Uniqure	First data from ph3 Hope-B trial in haemophilia B	LBA-6
Giroctocogene fitelparvovec	Sangamo/Pfizer	Haemophilia A, Alta trial, 11 pts, not clear what the cutoff is	671
DTX201/BAY 2599023	Bayer/Ultragenyx	FVIII gene therapy, first-in-human trial, <22mth data	1539
CTX001	Crispr/Vertex	2 SCD subjects free of crises at 12mth & 3mth, generating total haemoglobin of ~10g/dl	4
Oxbryta	Global Blood	72-week data from pivotal Hope study in SCD	1716
FT-4202	Forma Therapeutics	Jul 2020 data cut, 3 SCD patients	679
Mitapivat	Agios	Jul 2020 data cut, 9 SCD patients	681
RP-L102	Rocket Pharmaceuticals	Fanconi anaemia gene therapy, 2 pts at Aug 2020 data cut; registrational trial under way	674
RP-L201	Rocket Pharmaceuticals	LAD-I gene therapy, 2 pts; US filing due 2022	675

As with many Ash presentations, up-to-date details will only be made available at the meeting itself. In haemophilia A Sangamo and Ultragenyx investors will look for updated results from studies of the gene therapies giroctocogene fitelparvovec and BAY 2599023 respectively.

Ash also promises a significant focus on sickle cell disease; Crispr/Vertex's CTX001 study had already made waves when its abstract was first disclosed, and it is now apparent that it has been selected for presentation at an Ash press briefing too (*Ash 2020 preview – early winners and losers, November 6, 2020*).

Agios and Forma will present sickle cell data on their duelling pyruvate kinase R activators, mitapivat and FT-4202 respectively. Investors will hope for more data than each abstract's July 2020 cutoff discloses.

And a relatively little-known gene therapy player, Rocket Pharmaceuticals, will hope to make a splash with data on two rare disease projects, RP-L102 for Fanconi anaemia and RP-L201 for leukocyte adhesion deficiency-I. A poster on the first two patients treated with the former asset had sent Rocket up 63% over the period of last year's Ash meeting.

Though fund managers' end-of-year portfolio rationalisations often cause a post-Ash lull some investors will remain hopeful once the meeting gets under way.

Ash 2020 will take place in virtual format on December 5-8.