Evaluate Vantage

June 27, 2018

Global Blood launches bold bid for early sickle cell approval

Amy Brown

The main drawback of Global Blood Therapeutics' new plan to speed voxelotor to market is that the company might inadvertently put the sickle cell disease project into the slow lane.

It is hard to tell whether this will be the case; shares in the California drug developer initially fell as much as 13% this morning but then rose on news that it has begun talking to the US FDA about accelerated approval. This will be based on results from part A of the phase III Hope study, though mixed data from the trial, also released today, do not help build confidence in the strategy.

In fact GBT's strategy as it was previously understood seems to have been largely rewritten. In the past the company has played down the potential for accelerated approval, and has said that part B of the Hope study would use either patient-reported outcomes or vaso-occlusive crises as a secondary endpoint.

Success on at least one of these measures was presumed to be vital for approval. GBT has also previously said that they would be important in discussions with payers when it came to pricing.

A different tone emerged today on a conference call, with executives talking down the importance of these endpoints – on neither of which, in part A of Hope, voxelotor managed to generate meaningful data. Instead they emphasised the significance of change in haemoglobin levels, the primary endpoint of part A, on which voxelotor showed a statistically significant increase at both doses tested.

At the highest dose voxelotor performed much better than many had hoped: 58% of patients taking the 1,500mg dose achieved a greater than 1g/dl increase in haemoglobin at 12 weeks ($p<0.0001$). At the lower 900mg dose this was achieved by 38% of patients, versus 9% of placebo recipients ($p=0.0021$).

This result is certainly encouraging, and GBT went to great lengths to point out the inverse correlation between haemoglobin levels and morbidity and mortality among sickle cell patients. Chronic haemolytic anaemia substantially increases a patient's chance of stroke and renal failure, and by changing the biology of the disease with voxelotor lives can be improved and extended, executives pledged.

Missed opportunity?

GBT executives described discussions with the FDA as very encouraging, and said a decision on whether an accelerated approval is possible should come before the end of the year. The full data from Hope part A should also be presented by then – probably at Ash – setting up December as a critical month for the company.

A further 100 patients will have been enrolled into part A by then, giving the company data from around 250 patients to hand to the FDA. At this stage the start of Part B is on hold, meaning that should the regulator say no GBT will have lost several months of development time.

For this accelerated plan to work, GBT essentially needs the regulator to accept that haemolytic anaemia endpoints are more important than counting pain events – and on the call executives certainly gave the impression that this was the case. It also has on its side a relatively clean safety profile, and the huge unmet need in sickle cell disease.

While the part A data did not show a statistical improvement in the rate of vaso-occlusive crises, numerically fewer episodes occurred in both voxelotor groups than with placebo. The company blamed limited patient follow-up for the failure, a conclusion with which the regulator will presumably have to concur to sanction an accelerated approval.

Still, it should not be overlooked that GBT has given up on the opportunity to continue with a controlled, rigorous phase III trial, which would have yielded results next year anyway.

The welcoming stance of today's FDA improves voxelotor's chances of winning accelerated approval. Whether the project will go on to establish a disease modifying role in sickle cell disease is another question entirely.

To contact the writer of this story email Amy Brown in London at AmyB@epvantage.com or follow @ByAmyBrown on Twitter

More from Evaluate Vantage

Evaluate HQ
44-(0)20-7377-0800

Evaluate Americas
+1-617-573-9450

Evaluate APAC
+81-(0)80-1164-4754