Evaluate Vantage

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Bluebird sings sweet music to the ears of investors

Amy Brown

The 62% surge in Bluebird Bio shares this morning underlines the extent to which data presented at ASH last night surpassed even sky-high expectations. The advance is even more remarkable when considering that only eight patients have been treated to date, and only four have sufficiently advanced through trials to be evaluable.

Two on-going studies are testing Bluebird's gene therapy LentiGlobin, which promises to help blood transfusion-dependent patients with genetic disorders generate functioning haemogloblin. The unequivocally positive results spurred speculation that the technology represents a cure after only one treatment, a bold conclusion to draw at this stage of the game.

Of course if this does turn out to be the case, then the $870m added to Bluebird's valuation so far today will look conservative. In early trade shares were at $79 – the stock floated at $17 in June – and multiple analysts have already hiked price targets to $100 or more in the wake of the data.

However the excitement also reflects LentiGlobin's potential beyond beta-thalassemia, the rare genetic disorder in which data has been generated to date. Sickle-cell disease, a similar but relatively much more common condition, represents a multbillion-dollar opportunity – $50-$100bn in the US alone, according to Piper Jaffray. Prior to ASH even the bullish sellside community had shied away from attributing any value to this setting.

Analysts estimate that treating beta-thalassemia could generate peak sales of around $1bn for Bluebird. And many believe that this opportunity alone now supports a bigger valuation than even today's heftier market cap – Suntrust Robinson raised their price target from $57 to $115, saying they continue to exclude any impact from sickle cell disease.

Encouraging start

Whatever the eventual outcome, the data presented at ASH were highly encouraging on both efficacy and safety measures.

The Northstar or HGB-204 study is being conducted in 15 patients with beta-thalasseamia major; five have undergone transfusion with LentiGlobin to date. Of the two from whom readings are possible, both are producing steadily increasingly amount of beta-globin – the component part of haemoglobin that is affected by the disorder – and have not needed transfusions for five and three months.

Even more encouraging was the fact that one had the most severe genotype of the condition, beta-0/beta-0, or Cooley's anaemia; these patients produce almost no beta-globin and are therefore considered a big test of the therapy's potency.

The second study, HGB-205, is being conducted in France and is seeking seven patients with either beta-thalassemia or sickle cell disease. Two patients with the former condition have been recruited to date and now have near-normal haemoglobin levels for an adult – they have not needed transfusions for 12 and nine months, respectively.

The first patient with sickle cell has also been recruited and achieved neutrophil engraftment, Bluebird revealed, although any information on haemoglobin production is not yet available. Further updates on the progress of this patient will be a major focus in the coming months.

Flying high

Drawing firm conclusions from data in four patients is a risky game. But LentiGlobin to date appears to have done what it is supposed to do – replace a faulty gene with a functioning version – and even reducing the frequency of life-saving blood transfusions would be a huge step forward for these patients.

Over the coming months the company will be hoping to show that these responses are durable, without the

development of unwanted side effects. No serious gene therapy adverse events were reported at ASH, and importantly no evidence of “clonal dominance”, which would indicate the development of leukaemia.

It is still too early to judge the ultimate potential of this technique. But in terms of a first look at what its technology can do, Bluebird cannot have hoped for a stronger showing.

Trial name	Trial ID
HGB-204 (Northstar)	NCT01745120
HGB-205	NCT02151526

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