bluebird bio Presents Data from Phase 1/2 HGB-206 Group C Study Demonstrating LentiGlobin™ Gene Therapy for Sickle Cell Disease (SCD) Produces Anti-sickling Haemoglobin Contributing 40% or More to Total Haemoglobin Following Six Months of Treatment[1]

No reports of acute chest syndrome (ACS) or serious vaso-occlusive crisis (VOCs) at up to 21 months post-LentiGlobin treatment in Group C patients[1]

ZUG, Switzerland—Dec. 7, 2019— bluebird bio, GmbH. (Nasdaq: BLUE) today announced updated results from Phase 1/2 HGB-206 Group C clinical study of its LentiGlobin gene therapy for patients with sickle cell disease (SCD) at the 61st American Society of Hematology (ASH) Annual Meeting in Orlando, Florida, USA.[1]

"At ASH, the growing body of data from our clinical studies of LentiGlobin for SCD reflects results from 26 treated patients with up to four years of follow-up," said David Davidson, M.D., chief medical officer, bluebird bio. "We continue to observe patients treated in Group C producing high levels of gene-therapy derived anti-sickling haemoglobin, HbA^{T87Q}, accounting for at least 40% of total haemoglobin in those with six or more months of follow-up, and exploratory assays show that HbA^{T87Q} is present in most red blood cells of treated patients. The robust production of HbA^{T87Q} was associated with substantial reductions of sickle haemoglobin, HbS, as well as improvement in key markers of haemolysis. Most importantly, patients in Group C have not experienced any episodes of ACS or serious VOC following LentiGlobin for SCD treatment."

SCD is a serious, progressive and debilitating genetic disease caused by a mutation in the β-globin gene that leads to the production of abnormal sickle haemoglobin (HbS), causing red blood cells (RBCs) to become sickled and fragile, resulting in chronic haemolytic anaemia, vasculopathy and painful vaso-occlusive crises (VOCs).[2,3,4,5,6] For adults and children living with SCD, this can mean unpredictable, painful episodes due to vaso-occlusion as well as other acute complications—such as acute chest syndrome (ACS), stroke and infections, which can contribute to early mortality in these patients.[5,7,8]

As of 26 August 2019, 17 of the 49 patients with SCD enroled in the ongoing open-label Phase 1/2 HGB-206 study have been treated with LentiGlobin gene therapy, with the longest follow-up at 21 months.[1] 12 of the 17 treated patients in Group C had at least six months of follow-up at the time of the data cut-off.[1] In these patients, median levels of gene therapy-derived anti-sickling haemoglobin, HbA^{T87Q}, was at least 40% of total haemoglobin[1] and total haemoglobin and HbA^{T87Q} levels ranged from 9.3-15.2 g/dL and 2.7-9.0 g/dL, respectively, at last visit. None required regular RBC transfusions post-treatment.[1]

Sustained expression of gene therapy-derived haemoglobin in patients in Group C resulted in reduced levels of sickling haemoglobin that were approaching the levels in people who carry only one gene for sickle cell disease, suggesting that LentiGlobin treatment is improving biological markers of the disease.[2,9]

9 of the 12 patients with at least six months of follow-up who had four or more VOC or ACS events in the two years prior to treatment, reported a median annualised rate of zero VOC or ACS events at up to 21 months post-treatment.[1]

The results from Group C were reinforced by findings presented from exploratory assays designed to assess the relationship between LentiGlobin characteristics and RBC physiology.[10] The assays performed in samples from a subset of patients from Groups A, B and C in HGB-206 found that on average, 80% or more of patient RBCs contained HbA^{T87Q} six months after treatment.[10] This is indicative of a pan-cellular distribution of HbA^{T87Q} believed to be critical to LentiGlobin's disease modifying effect in SCD.[10]

As of the data cut-off date, the safety data from Group C in HGB-206 are reflective of underlying SCD, the known side effects of haematopoietic stem cell (HSC) collection and myeloablative conditioning, including serious events of nausea and vomiting, affecting 11.8% of patients respectively.[1] One mild, non-serious event of hot flush was reported that the investigator considered to be possibly related to LentiGlobin.[11]

About LentiGlobin for sickle cell disease

LentiGlobin is an investigational gene therapy being studied as a potential treatment for SCD. bluebird bio's clinical development programme for LentiGlobin for SCD includes the ongoing Phase 1/2 HGB-206 study.

LentiGlobin for SCD adds functional copies of a modified form of the β-globin gene ($\beta^{A\text{-}T87Q}$-globin gene) into a patient's own HSCs.[12] Once patients have the $\beta^{A\text{-}T87Q}$-globin gene, they have the potential to make functional RBCs, with the goal of reducing sickled RBCs, haemolysis, and other complications.[2]

LentiGlobin received Orphan Medicinal Product designation from the European Commission for the treatment of SCD.

The U.S. Food and Drug Administration granted Orphan Drug status and Regenerative Medicine Advanced Therapy designation for LentiGlobin for the treatment of SCD.

bluebird bio is conducting a long-term safety and efficacy follow-up study (LTF-303) for people who have participated in bluebird bio-sponsored clinical studies of LentiGlobin for SCD. For more information visit: clinicaltrials.gov and use identifier NCT02633943 for LTF-303.

About bluebird bio, Inc.

bluebird bio is pioneering gene therapy with purpose. From our Cambridge, Mass., headquarters, we're developing gene therapies for severe genetic diseases and cancer, with the goal that people facing potentially fatal conditions with limited treatment options can live their lives fully. Beyond our labs, we're working to positively disrupt the healthcare system to create access, transparency and education so that gene therapy can become available to all those who can benefit.

bluebird bio is a human company powered by human stories. We're putting our care and expertise to work across a spectrum of disorders including cerebral adrenoleukodystrophy, sickle cell disease, β-thalassaemia and multiple myeloma, using three gene therapy technologies: gene addition, cell therapy and (megaTAL-enabled) gene editing.

bluebird bio has additional nests in Seattle, Wash.; Durham, N.C.; Zug, Switzerland; Munich, Germany; Milan, Italy; Utrecht, the Netherlands; Hampshire, United Kingdom; and Paris, France.

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