bluebird bio Presents New Data for LentiGlobin® Gene Therapy for Sickle Cell Disease (SCD) at 24th European Haematology Association (EHA) Congress

In patients who were at least six months post-treatment with LentiGlobin for severe SCD, median level of abnormal sickle haemoglobin (HbS) was reduced to ≤50 percent of total Hb

At up to 15 months post-treatment with LentiGlobin there were no reports of serious vaso-occlusive crisis or acute chest syndrome in Group C

ZUG, Switzerland —14 June, 2019—bluebird bio, Inc. announced new data from patients in Group C of its ongoing Phase 1/2 HGB-206 study of the company's investigational LentiGlobin® gene therapy for severe sickle cell disease (SCD) today at the 24th European Haematology Association (EHA) Congress in Amsterdam, the Netherlands.

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 events (VOEs). For adults and children living with SCD this means unpredictable, episodes of excruciating pain 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.

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

"The latest Group C data from our Phase 1/2 study show robust production of gene therapy-derived-anti-sickling haemoglobin HbA^{T87Q}, such that patients with six or more months of follow-up after treatment with LentiGlobin, for sickle cell disease had median sickle haemoglobin levels reduced to 50 percent or less of total, in the absence of blood transfusions. The potential for gene therapy with LentiGlobin to fundamentally alter the pathophysiology of sickle cell disease was also supported by the normalisation of haemolysis markets, increase in total haemoglobin, and substantial reduction in vaso-occlusive crises relative to baseline," said David Davidson, M.D., chief medical officer, bluebird bio. "Further insight into these encouraging clinical results was provided by findings from an exploratory assay used to evaluate the expression of HbA^{T87Q}, which demonstrated 70 percent or more of patient red blood cells contain HbA^{T87Q} at nine months after treatment."

Phase 1/2 study: HGB-206
HGB-206 is an ongoing, Phase 1/2 open-label study designed to evaluate the efficacy and safety of LentiGlobin gene therapy for severe SCD that includes three treatment cohorts: Group A, B and C. As of March 7, 2019, 25 patients were enrolled and a total of 13 patients had been treated with LentiGlobin in Group C, with a median post-treatment follow-up of nine months (1.0 – 15.2 months).

"The severity of sickle cell disease is not always recognised, and many people are unaware that individuals are debilitated by the effects of sickle cell disease." Julie Kanter, M.D., University of Alabama

at Birmingham, Birmingham, Alabama. “Group C of the Phase 1/2 HGB-206 study of LentiGlobin now includes multiple patients with at least one year of follow-up, and in these individuals, many with a history of vaso-occlusive crises, their symptoms appear to be resolving. There have been no incidents of acute chest syndrome or serious vaso-occlusive crises reported and many of their labs are approaching normal.”

Eight of the 13 treated patients in Group C had at least six months of follow-up at the time of the data cut-off. In these patients, production of gene therapy-derived haemoglobin (HbA^{T87Q}) ranged from 4.5 – 8.8 g/dL and total unsupported haemoglobin levels ranged from 10.2 – 15.0 g/dL at last study visit.

The median concentration of HbA^{T87Q} continued to increase, accounting for ≥50 percent of total haemoglobin in patients with at least 12 months of follow up (n=4).

No ACS or serious vaso-occlusive crisis VOCs was reported in patients in Group C at up to 15 months post-treatment with LentiGlobin. In an exploratory analysis, key markers of haemolysis, including reticulocyte counts, lactate dehydrogenase (LDH) and total bilirubin concentration trended toward normal levels.

As of the data cut-off date, the safety data from all patients in HGB-206 are reflective of underlying SCD, the known side effects of haematopoietic stem cell (HSC) collection and myeloablative conditioning. There have been no serious adverse events (SAEs) related to LentiGlobin for SCD. One mild, non-serious event of hot flush was reported that the investigator considered to be related to LentiGlobin for SCD; it occurred and resolved on the day of drug product infusion and did not require treatment.

Established tools, including high-performance liquid chromatography (HPLC) are used to measure the amount of Hb^{T87Q} in a blood sample. In order to detect HbA^{T87Q} and HbS protein expression at a cellular level, bluebird bio has utilised a new exploratory assay to demonstrate the pancellular expression of HbA^{T87Q} in patients treated with LentiGlobin. The assay enables detection of HbA^{T87Q} and HbS protein expression at a cellular level. Results from this assay, showed that in samples from five patients who were at least nine months post treatment, on average at least 70 percent of each patient’s RBCs expressed HbA^{T87Q}.

About LentiGlobin for severe Sickle Cell Disease
LentiGlobin for severe sickle cell disease (SCD) is an investigational gene therapy being studied as a potential treatment for severe SCD. bluebird bio’s clinical development programme for LentiGlobin for SCD includes the ongoing Phase 1/2 HGB-206 study.

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.

LentiGlobin for SCD 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.

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 by researching cerebral adrenoleukodystrophy, sickle cell disease, transfusion-dependent 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. Our European headquarters are in Zug, Switzerland, and we have offices in France, Germany, Italy, the UK and the Netherlands.

LentiGlobin is a trademark of bluebird bio.

Forward-Looking Statements
This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: the risk that the efficacy and safety results from our prior and ongoing clinical trials of LentiGlobin for SCD will not continue or be repeated in our ongoing or planned clinical trials of LentiGlobin for SCD; the risk that the current or planned clinical trials of LentiGlobin for SCD will be insufficient to support regulatory submissions or marketing approval in the US and EU; the risk that the production of $Hb^{A\text{-}T87Q}$ may not be sustained over extended periods of time; and the risk that we may not secure adequate pricing or reimbursement to support continued development or commercialisation of LentiGlobin for SCD following regulatory approval. For a discussion of other risks and uncertainties, and other important factors, any of which could cause our actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in our most recent Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in our subsequent filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and bluebird bio undertakes no duty to update this information unless required by law.

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