bluebird bio Presents Long-Term Efficacy and Safety Data from Clinical Studies of LentiGlobin® Gene Therapy for Transfusion-Dependent β-Thalassaemia (TDT) at 24th European Haematology Association (EHA) Congress

Up to 3.8 years of transfusion independence in Phase 1/2 Northstar (HGB-204) study in patients with TDT who do not have a β^0/β^0 genotype

Four of five evaluable patients achieved transfusion independence (which is the primary endpoint) in ongoing Phase 3 Northstar-2 (HGB-207) study of patients with TDT who do not have a β^0/β^0 genotype

In patients who were free from transfusions for at least three months total haemoglobin levels were 10.2 – 13.6 g/dL in the ongoing Phase 3 Northstar-3 (HGB-212) study in patients with TDT who have a β0/β0 genotype or IVS-1-110 mutation

ZUG, Switzerland—14 June, 2019—bluebird bio, Inc. announced updated results from the completed Phase 1/2 Northstar (HGB-204) study and new data from the Phase 3 Northstar-2 (HGB-207) and Phase 3 Northstar-3 (HGB-212) clinical studies of its LentiGlobin™ gene therapy for patients with transfusion-dependent β-thalassaemia (TDT), at the 24th European Haematology Association (EHA) Congress in Amsterdam, the Netherlands.

"The maturing data from our clinical studies of LentiGlobin for TDT show that patients across genotypes are able to achieve and maintain transfusion independence, with production of gene therapy-derived haemoglobin HbA^{T87Q}, extending for years," said David Davidson M.D., chief medical officer, bluebird bio. "In patients who achieve transfusion independence, we have observed decreased liver iron concentration over time, and improved markers of erythropoiesis, demonstrating the transformative disease-modifying potential of gene therapy with TDT."

TDT is a severe genetic disease caused by mutations in the β-globin gene that result in reduced or absent haemoglobin (Hb). In order to survive, people with TDT maintain Hb levels through lifelong chronic blood transfusions. These transfusions carry the risk of progressive multi-organ damage due to unavoidable iron overload.

LentiGlobin for β-thalassaemia addresses the underlying genetic cause of TDT by adding 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). This means there is no need for donor HSCs from another person as is required for allogeneic HSC transplantation (allo-HSCT). Once a patient has the $\beta^{A\text{-}T87Q}$ globin gene they have the potential to produce HbA^{T87Q}, which is gene therapy- derived-haemoglobin, at levels that eliminate or significantly reduce the need for transfusions.

bluebird bio's clinical development programme for LentiGlobin in TDT includes studies across patient genotypes including those who do not have a β^0/β^0 genotype as well as those with a β^0/β^0 genotype.

"Patients living with β-thalassaemia who have a β^0/β^0 genotype or an IVS-I-110 mutation typically have low levels of endogenous haemoglobin," said Andreas Kulozik, M.D., Ph.D., Heidelberg University Hospital, Heidelberg, Germany. "Transfusion independence is a goal for the treatment of TDT, regardless of genotype. Early results from the ongoing Phase 3 study in patients with β^0/β^0 genotype or an IVS-I-110 mutation show gene-therapy-derived-haemoglobin significantly contributes to improved total haemoglobin levels."

Northstar (HGB-204)

The results reported for the completed Phase 1/2 Northstar (HGB-204) study reflect data as of December 13, 2018; of the 18 patients in the study, 10 patients do not have a β^0/β^0 genotype and eight have a β^0/β^0 genotype. All 18 patients have completed the two-year study and enrolled in the long-term follow-up study, LTF-303.

Eight of 10 treated patients who do not have a β^0/β^0 genotype achieved transfusion independence (TI), meaning they had not received a transfusion for at least 12 months or more and maintained a weighted average Hb≥9 g/dL.

These eight patients had a median weighted average Hb during TI of 10.3 g/dL (min – max: 9.3 – 13.2 g/dL) and continued to maintain TI up to 45 months. The patient follow-up period is calculated from infusion of LentiGlobin to last study visit.

In patients who have a β^0/β^0 genotype, three of the eight achieved TI and maintained a median weighted average Hb ranging from 9.5 – 10.1 g/dL for a median duration of 16.4 months (min – max: 16.1 – 20.8 months).

An exploratory assessment was conducted to assess liver iron concentration (LIC) in the 11 patients from the Northstar study who achieved TI. Increased iron levels are a consequence of frequent transfusions. High iron levels can cause organ damage, which many patients with TDT are at risk of and must manage through chelation regimens.

LIC was measured at baseline and then every 12 months after treatment with LentiGlobin. Patients re-initiated iron chelation therapy a median of 13 months after LentiGlobin infusion (min – max: 2 – 16 months). Over time, LIC began to decrease in all 11 patients with the largest decrease observed in patients who had 48 months of data available (n=4). A median 56 percent reduction (min – max: 38 – 83 percent) was reported in these four patients.

Northstar-2 (HGB-207) Efficacy

As of December 13, 2018, 20 patients who do not have β^0/β^0 genotypes have been treated in the Phase 3 Northstar-2 study. Patient age ranged from 8 – 34 years, with five paediatric (<12 years) and 15 adolescents/adults (≥12 years) patients.

Four of five evaluable patients achieved TI and maintained a median weighted average Hb of 12.4 g/dL (min – max: 11.5 – 12.6 g/dL). These four patients continued to maintain TI for a median duration of 13.6 months (min – max: 12 – 18.2 months) at the time of the data cut off.

Thirteen of 14 patients with at least three months follow-up, 13 were free from transfusions for at least three months. Total Hb levels in these patients ranged from 8.8 – 13.3 g/dL at the time of the last study visit. HbA^{T87Q} levels were stable over time in patients who were free from transfusions; at month 6 (n=10) median Hb^{AT87Q} was 9.5g/dL and a month 12 (n=7) median Hb^{AT87Q} was 9.3g/dL.

An exploratory analysis was conducted with bone marrow from seven patients with 12 months of follow-up after treatment. The samples were evaluated for cellularity and myeloid to erythroid ratio. A low myeloid to erythroid ratio is a key feature of dyserythropoiesis, or abnormal bone marrow red blood cell production, characteristic of patients with TDT. In these seven patients, all of whom had stopped chronic transfusions, an increase in the myeloid to erythroid ratio was observed, suggesting improvement in RBC production.

Northstar-3 (HGB-212) Efficacy
As of April 12, 2019, 11 patients with TDT and a β^0/β^0 genotype or an IVS-I-110 mutation had been treated in the Phase 3 Northstar-3 study.

The one patient evaluable for TI achieved and maintained it and had a total Hb of 13.6g/dL13.6 g/dL at the month 16 follow-up.

Five patients had stopped transfusions for at least three months and had Hb levels of 10.2– 13.6 g/dL at the time of the last study visit (5 – 16 months post-treatment). Of these patients, all of those who reach six months of follow-up (n=4) had HbA^{T87Q} levels of at least 8g/dL.

LentiGlobin for TDT Safety
Non-serious adverse events (AEs) observed during clinical studies that were attributed to LentiGlobin for TDT were hot flush, dyspnoea, abdominal pain, pain in extremities and non-cardiac chest pain. One serious adverse event (SAE) of thrombocytopenia was considered possibly related to LentiGlobin.

Additional AEs observed in clinical studies were consistent with the known side effects of HSC collection and bone marrow ablation with busulfan including SAEs of veno-occlusive disease.

As of the data cut-off dates stated above, a total of 49 paediatric, adolescent and adult patients with TDT and a non-β^0/β^0 or β^0/β^0 genotype, including patients with IVS-I-110 mutations, have been treated with LentiGlobin for TDT in the Northstar, Northstar-2 and Northstar-3 studies.

About LentiGlobin for β-Thalassaemia
The European Commission (EC) granted conditional marketing authorisation for LentiGlobin for TDT, to be marketed as Zynteglo® (autologous CD34+ cells encoding $\beta^{A\text{-}T87Q}$-globin gene) gene therapy, for patients 12 years and older with TDT who do not have a β^0/β^0 genotype, for whom haematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte antigen (HLA)-matched related HSC donor is not available.

Zynteglo 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 a patient has the $\beta^{A\text{-}T87Q}$-globin gene they

have the potential to produce HbA^{T87Q}, which is gene therapy-derived-haemoglobin, at levels that eliminate or significantly reduce the need for transfusions. Upon engraftment and achievement of transfusion independence, effects of Zynteglo are expected to be life-long.

The EMA previously granted Priority Medicines (PRIME) eligibility and Orphan Medicinal Product designation to Zynteglo for the treatment of TDT. Zynteglo is also part of the EMA's Adaptive Pathways pilot programme, which is part of the EMA's effort to improve timely access for patients to new medicines.

The U.S. Food and Drug Administration (FDA) also granted Zynteglo Orphan Drug status and Breakthrough Therapy designation for the treatment of TDT.

LentiGlobin for TDT continues to be evaluated in the ongoing Phase 3 Northstar-2 and Northstar-3 studies and the long-term follow-up study LTF-303. For more information about the ongoing clinical studies visit clinicaltrials.gov and use identifier NCT01745120 for Northstar (HGB-204), NCT02906202 for Northstar-2 (HGB-207), NCT03207009 for Northstar-3 (HGB-212) and 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 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.

Zynteglo and LentiGlobin are trademarks of bluebird bio.

The full common name for Zynteglo: A genetically modified autologous CD34+ cell enriched population that contains haematopoietic stem cells transduced with lentiviral vector encoding the $\beta^{A\text{-}T87Q}$-globin gene.

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 TDT will not continue or be

repeated in our ongoing or planned clinical trials of LentiGlobin for TDT; the risk that the current or planned clinical trials of LentiGlobin for TDT will be insufficient to support future regulatory submissions in the US and EU or additional marketing authorisations; 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 TDT. 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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