bluebird bio Receives Positive Opinion from CHMP for Zynteglo™ (autologous CD34+ cells encoding β $^{A\text{-}T87Q}$globin gene) Gene Therapy for Patients 12 Years and Older with Transfusion-Dependent β-Thalassaemia (TDT) and Who Do Not Have a β^0/β^0 Genotype

First gene therapy to receive positive CHMP opinion in the EU for a subset of adult and adolescent patients with TDT

Treatment has been shown to help eliminate the need for chronic blood transfusions in adult and adolescent patients with TDT who do not have a β^0/β^0 Genotype

This is bluebird bio's first gene therapy submitted for assessment by a regulatory authority

CAMBRIDGE, Mass.- March 29, 2019- bluebird bio, Inc. (Nasdaq: BLUE) announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending conditional marketing authorisation for Zynteglo™ (autologous CD34+ cells encoding β $^{A\text{-}T87Q}$-globin gene, formerly known as LentiGlobin™). This is a gene therapy for patients 12 years and older with transfusion-dependent β-thalassaemia (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.

Andrew Obenshain, bluebird bio European General Manager commented: "We are delighted that our first gene therapy to be submitted for regulatory approval has achieved a positive CHMP opinion. It is our aspiration that this will enable people living with TDT to produce haemoglobin at sufficient levels to reduce or eliminate the need for chronic blood transfusions. This is an important step forward in making our therapy available to patients across Europe and we would like to acknowledge the role of the TDT community, patients and clinical investigators in helping us to get to this point. We look forward to the upcoming decision from the European Commission over the next few months."

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

bluebird's gene therapy was reviewed under an accelerated assessment timeline as part of the EMA's Priority Medicines (PRIME) and Adaptive Pathways programmes, which supports medicines that may offer a major therapeutic advantage over existing treatments, or benefit patients without treatment options. The CHMP's positive opinion will now be reviewed by the European Commission (EC), which has the authority to grant a marketing authorisation in the European Union. A CHMP positive opinion is one of the final steps before the EC decides on whether to authorise a new medicine. A final decision is anticipated in the second quarter of 2019.

"For many of my patients, living with TDT means a lifetime of chronic blood transfusions, iron chelation therapy and supportive treatments to manage anaemia and other serious complications of this disease," said Professor Franco Locatelli, M.D., Ph.D., Professor of Pediatrics, Sapienza University of Rome, Italy and Director, Department of Pediatric Hematology/Oncology and Cell and Gene Therapy, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy. "The burden placed on these patients and their families is significant. It extends beyond immediate health implications to their daily lives, which are affected by the symptoms, hospitalisations and necessary chronic care required for TDT."

"The present management of TDT, including regular blood transfusions every two to four weeks and daily iron chelation therapy has many psychological and social consequences, including marginalisation and isolation. And, in many patients TDT-related morbidities can lead to a shortened life span. Therefore, it is with great anticipation and eagerness that the international patient community has closely followed the dynamic rejuvenation of scientific interest and research of gene therapy in TDT over the last few years," said Dr Androulla Eleftheriou, Thalassaemia International Federation Executive Director. "Thus, the potential approval of a gene therapy brings hope that we can dramatically change the course of this disease and the health and quality of lives of patients with TDT."

The treatment approach adds copies of a modified form of β-globin gene (β-globin A^{T87Q}) 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). A patient's HSCs are collected and removed from the body through a process called apheresis. These HSCs are taken to a lab where a lentiviral vector is used to insert one or more copies of the $\beta^{A\text{-}T87Q}$-globin gene into the patient's HSCs. This step is called transduction. Before the modified HSCs are returned to the patient, they receive chemotherapy to prepare their bone marrow to receive the modified HSCs, which are returned through an intravenous infusion. Once a patient has the $\beta^{A\text{-}T87Q}$-globin they have the potential to produce HbA^{T87Q}, which is gene therapy derived-haemoglobin, at levels that reduce or eliminate the need for transfusions.

Data Supporting Clinical Profile of Zynteglo

The positive CHMP opinion is supported by efficacy, safety and durability data from the completed Phase 1/2 HGB-205 study and Phase 1/2 Northstar (HGB-204) study as well as available data from the ongoing Phase 3 Northstar-2 (HGB-207) and Northstar-3 (HGB-212) studies, and the long-term follow-up study LTF-303.

As of September 14, 2018, data from Phase 1/2 Northstar showed that 80 percent (n=8/10) of patients who do not have a β^0/β^0 genotype achieved transfusion independence, meaning they had not received a transfusion for at least 12 months and maintained a weighted average haemoglobin ≥9 g/dL. These eight patients had maintained transfusion independence for a median duration of 38 months (21 – 44 months) at the time of data cut-off.

In the Phase 3 Northstar-2 and Northstar-3 studies a refined manufacturing process was used intended to further improve on the clinical results observed in the Northstar study. As of September 14, 2018, the median (min, max) total haemoglobin for patients six months after infusion in the Northstar-2 study (n=10) was 11.9 (8.4, 13.3) g/dL.

Patients continue to be evaluated in the ongoing Phase 3 Northstar-2 and Northstar-3 studies and the long-term follow-up study LTF-303.

Non-serious adverse events (AEs) observed during clinical trials 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 this therapy.

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

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 and 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 is: A genetically modified autologous CD34+ cell enriched population that contains haematopoietic stem cells transduced with lentiviral vector encoding the β^{A-T87Q}-globin gene.

Forward-Looking Statements

This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including statements regarding the Company's plans and expectations for the development, regulatory approval, and commercialization for the Zynteglo™ (autologous CD34+ cells encoding β^{A-T87Q}-globin gene, formerly LentiGlobin™) to treat transfusion-dependent β-thalassaemia, and the potential implications of clinical data for patients. 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 our MAA submitted for Zynteglo may not be approved by the European Commission when expected, or at all; the risk that the efficacy and safety results from our prior and ongoing clinical trials of Zynteglo will not continue or be repeated in our ongoing or planned clinical trials of Zynteglo; the risk that the current or planned clinical trials of Zynteglo will be insufficient to support regulatory submissions or marketing approval in the US and EU; the risk that the production of HbA^{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 commercialization of Zynteglo 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-K, 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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