bluebird bio Announces Launch in Germany of Zynteglo™▼(autologous CD34+ cells encoding $\beta^{A\text{-}T87Q}$-globin gene)

First qualified treatment centre established at University Hospital of Heidelberg

First agreements with statutory health insurance funds that provide coverage for 50% of the insured population in Germany will utilise an innovative value-based payment model to provide coverage for the treatment

ZUG, Switzerland.—(BUSINESS WIRE)— 13 January 2020— bluebird bio, Inc. (Nasdaq: BLUE) announced the launch in Germany of Zynteglo (autologous CD34+ cells encoding $\beta^{A\text{-}T87Q}$-globin gene), a one-time 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. This is the first time that the treatment will be available in the European Union.

TDT is a severe genetic disease caused by mutations in the β-globin gene that result in reduced or significantly reduced haemoglobin (Hb).[1,2] In order to survive, people with TDT maintain Hb levels through life-long chronic blood transfusions.[2,3] Regular transfusions cause iron overload leading to progressive multi-organ damage if not treated with chelation to remove excess iron from the body.[2,3]

Zynteglo is a one-time gene therapy that addresses the underlying genetic cause of TDT and offers patients the potential to become transfusion independent, which once achieved is expected to be lifelong.[4]

Due to the highly technical and specialised nature of administering gene therapy in rare diseases, bluebird bio is working with institutions that have expertise in stem cell transplant as well as in treating patients with TDT to create qualified treatment centres that will administer the treatment. bluebird bio has established a collaboration with University Hospital of Heidelberg, as the first qualified treatment centre in Germany.

In addition, bluebird has entered into value-based payment agreements with multiple statutory health insurances in Germany to help ensure patients and their healthcare providers have access to the treatment and that payers only pay if the therapy delivers on its promise. bluebird's proposed innovative model is limited to five payments made in equal instalments. After the first payment, four additional annual payments are only made if no transfusions are required for the patient.

"For many patients and families living with TDT, lifelong chronic blood transfusions are required in order to survive. We are thrilled to announce that the treatment will now be available for a subset of patients in the EU living with this severe disease," says Alison Finger, chief commercial officer, bluebird bio. "In addition to confirming manufacturing readiness of our partner, apceth Biopharma GmbH, the company has also submitted a dossier to the Joint Federal Committee (G-BA) in Germany for drug benefit assessment. We would like to thank our collaborators for their commitment in helping us transform the healthcare system to accept innovative payment models, to bring this potentially transformative therapy to patients, families and the providers who care for them."

About LentiGlobin for β-Thalassaemia (autologous CD34+ cells encoding $\beta^{A\text{-}T87Q}$-globin gene)
The European Commission granted conditional marketing authorisation for LentiGlobin for β-thalassaemia, 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.[4]

LentiGlobin was designed to address the underlying genetic cause of TDT by adding functional copies of a modified form of the β-globin gene (βA-T87Q-globin gene) into a patient's own haematopoietic (blood) stem cells (HSCs).[4] Once a patient has the βA-T87Q-globin gene, they have the potential to produce HbAT87Q, which is gene therapy-derived haemoglobin, at levels that may eliminate or significantly reduce the need for transfusions.[4]

Non-serious adverse events (AEs) observed during the HGB-204, HGB-207 and HGB-212 clinical studies that were attributed to LentiGlobin for β-thalassaemia were hot flush, dyspnoea, abdominal pain, pain in extremities, thrombocytopenia, leukopenia, neutropenia and non-cardiac chest pain. One serious adverse event (SAE) of thrombocytopenia was considered possibly related to LentiGlobin for β-thalassaemia for TDT.

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.

The conditional marketing authorisation is valid in the 28-member states of the EU as well as Iceland, Liechtenstein and Norway. For details, please see the Summary of Product Characteristics (SmPC).[4]

The U.S. Food and Drug Administration (FDA) granted LentiGlobin for β-thalassaemia Orphan Drug status and Breakthrough Therapy designation for the treatment of TDT, but it is not approved in the United States. bluebird bio is engaged with the FDA in discussions regarding the requirements and timing of the various components of the rolling BLA submission and, subject to these ongoing discussions, the company is currently planning to complete the BLA submission in the first half of 2020.

LentiGlobin for β-thalassaemia continues to be evaluated in the ongoing Phase 3 Northstar-2 and Northstar-3 studies. For more information about the ongoing clinical studies, visit northstarclinicalstudies.com or clinicaltrials.gov and use identifier NCT02906202 for Northstar-2 (HGB-207) or NCT03207009 for Northstar-3 (HGB-212).

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 β-thalassaemia. For more information visit clinicaltrials.gov and use identifier NCT02633943 for LTF-303.

▼This medicinal product is subject to additional monitoring.

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.

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.

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 commercialization for ZYNTEGLO™ (autologous CD34+ cells encoding $\beta^{A\text{-}T87Q}$-globin gene, formerly LentiGlobin™ in TDT) to treat TDT, 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 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, or for additional patient populations in the EU; the risk that the production of HbA^{T87Q} may not be sustained over extended periods of time; the risk that we may not secure adequate pricing or reimbursement to support continued development or commercialization of ZYNTEGLO; the risk that our collaborations with qualified treatment centres will not continue or be successful; and that the risk that commercial patients treated with ZYNTEGLO will not achieve or maintain transfusion independence. 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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