bluebird bio Announces Temporary Suspension on Phase 1/2 and Phase 3 Studies of LentiGlobin Gene Therapy for Sickle Cell Disease (bb1111)

ZUG, Switzerland — Feb. 16, 2021 – bluebird bio, Inc. announced today that the company has placed its Phase 1/2 (HGB-206) and Phase 3 (HGB-210) studies of LentiGlobin gene therapy for sickle cell disease (SCD) (bb1111) on a temporary suspension due to a reported Suspected Unexpected Serious Adverse Reaction (SUSAR) of acute myeloid leukemia (AML).

In line with the clinical study protocols for HGB-206 and HGB-210, bluebird bio placed the studies on temporary suspension following a report received last week that a patient who was treated more than five years ago in Group A of HGB-206 was diagnosed with AML. The company is investigating the cause of this patient's AML in order to determine if there is any relationship to the use of BB305 lentiviral vector in the manufacture of LentiGlobin gene therapy for SCD. A second SUSAR of myelodysplastic syndrome (MDS) in a patient from Group C of HGB-206 was reported last week to the company and is currently being investigated.

No cases of hematologic malignancy have been reported in any patient who has received treatment with betibeglogene autotemcel for transfusion-dependent β-thalassemia (licensed as Zynteglo®▼ in the European Union and the United Kingdom), however because it is also manufactured using the same BB305 lentiviral vector used in LentiGlobin gene therapy for SCD, the company has decided to temporarily suspend marketing of Zynteglo while the AML case is assessed.

"The safety of every patient who has participated in our studies or is treated with our gene therapies is the utmost priority for us," said Nick Leschly, chief bluebird. "We are committed to fully assessing these cases in partnership with the healthcare providers supporting our clinical studies and appropriate regulatory agencies. Our thoughts are with these patients and their families during this time."

The independent safety review board monitoring the company's studies as well as the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) have been advised of these cases and bluebird bio will continue to work with regulatory agencies to complete its investigation.

About HGB-206 and HGB-210

HGB-206 is an ongoing, Phase 1/2 open-label study designed to evaluate the efficacy and safety of LentiGlobin gene therapy for sickle cell disease (SCD) that includes three treatment cohorts: Groups A, B and C. A refined manufacturing process designed to increase vector copy number (VCN) and further protocol refinements made to improve engraftment potential of gene-modified stem cells were used for Group C. Group C patients also received LentiGlobin for SCD made from HSCs collected from peripheral blood after mobilization with plerixafor, rather than via bone marrow harvest, which was used in Groups A and B of HGB-206.

HGB-210 is an ongoing Phase 3 single-arm open-label study designed to evaluate the efficacy and safety of LentiGlobin gene therapy for SCD in patients between two years and 50 years of age with sickle cell disease.

About LentiGlobin for SCD (bb1111)

LentiGlobin gene therapy for sickle cell disease (bb1111) is an investigational treatment being studied as a potential treatment for SCD. bluebird bio's clinical development program for LentiGlobin for SCD includes the completed Phase 1/2 HGB-205 study, the ongoing Phase 1/2 HGB-206 study, and the ongoing Phase 3 HGB-210 study.

The U.S. Food and Drug Administration granted orphan drug designation, fast track designation, regenerative medicine advanced therapy (RMAT) designation and rare pediatric disease designation for LentiGlobin for SCD.

LentiGlobin for SCD received orphan medicinal product designation from the European Commission for the treatment of SCD, and Priority Medicines (PRIME) eligibility by the European Medicines Agency (EMA) in September 2020.

bluebird bio is conducting a long-term safety and efficacy follow-up study (LTF-307) for people who have participated in bluebird bio-sponsored clinical studies of LentiGlobin for SCD. For more information visit: **clinicaltrials.gov** and use identifier NCT04628585 for LTF-307.

LentiGlobin for SCD is investigational and has not been approved in any geography.

About Zynteglo (betibeglogene autotemcel)

Betibeglogene autotemcel (beti-cel) is a one-time gene therapy that adds functional copies of a modified form of the β-globin gene ($\beta^{A\text{-}T87Q}$-globin gene) into a patient's own hematopoietic (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 adult Hb, at levels that may eliminate or significantly reduce the need for transfusions. In studies of beti-cel, transfusion independence (TI) is defined as no longer needing red blood cell transfusions for at least 12 months while maintaining a weighted average Hb of at least 9 g/dL.

The European Commission granted conditional marketing authorization (CMA) for beti-cel, marketed as Zynteglo™ gene therapy, for patients 12 years and older with transfusion-dependent β-thalassemia (TDT) who do not have a β^0/β^0 genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate, but a human leukocyte antigen (HLA)-matched related HSC donor is not available.

Non-serious adverse events (AEs) observed during clinical studies that were attributed to beti-cel included abdominal pain, thrombocytopenia, leukopenia, neutropenia, hot flush, dyspnea, pain in extremity, tachycardia and non-cardiac chest pain. One serious adverse event (SAE) of thrombocytopenia was considered possibly related to beti-cel.

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.

For details, please see the Summary of Product Characteristics (SmPC).

On April 28, 2020, the European Medicines Agency (EMA) renewed the CMA for beti-cel. The CMA for beti-cel is valid in the 27 member states of the EU as well as the UK, Iceland, Liechtenstein and Norway.

The U.S. Food and Drug Administration granted beti-cel Orphan Drug status and Breakthrough Therapy designation for the treatment of TDT. Beti-cel is not approved in the U.S. Beti-cel continues to be evaluated in the ongoing Phase 3 Northstar-2 (HGB-207) and Northstar-3 (HGB-212) studies.

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 Zynteglo.

▼ This medicinal product is subject to additional monitoring

About bluebird bio, Inc.

bluebird bio is pioneering gene therapy with purpose. From our Cambridge, Mass., headquarters, we're developing gene and cell 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: cerebral adrenoleukodystrophy, sickle cell disease, β-thalassemia and multiple myeloma, using gene and cell therapy technologies including gene addition, 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; Basingstoke, United Kingdom; Paris, France; and Athens, Greece.

▼ This medicinal product is subject to additional monitoring

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 timing and expectations regarding its investigation of the relationship of the AML and MDS events to the use of lentiviral vector BB305 in LentiGlobin gene therapy for SCD, and any myeloablation regimen used in connection with treatment. 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, many of which are beyond the Company's control. These risks and uncertainties include, but are not limited to: the risk that the Company may not be able to definitively determine whether the lentiviral vector BB305 used in LentiGlobin gene therapy for SCD and in betibeglogene autotemcel is related to the patient's AML in a timely manner, or at all; the risk that the lentiviral vector BB305 has caused insertional oncogenic events, including AML; the risk that insertional oncogenic events associated with lentiviral vector or additional MDS events associated with myeloablation will be discovered or reported over time; the risk that regulatory authorities may impose a clinical hold, in addition to our temporary clinical hold on the

HGB-206 and HGB-210 studies, or on additional programs; the risk that we may not be able to address regulatory authorities' concerns quickly or at all; the risk that we may not resume patient treatment with Zynteglo in the commercial context in a timely manner or at all; the risk that our lentiviral vector platform across our severe genetic disease programs may be implicated, affecting the development and potential approval of elivaldogene autotemcel; the risk that we may not be able to execute on our business plans, including our commercialization plans, meeting our expected or planned regulatory milestones, submissions, and timelines, research and clinical development plans, and in bringing our product candidates to market; and the risk that with the impact on the execution and timing of our business plans, we may not successfully execute our previously announced plans to spin off our oncology programs into an independent publicly-traded entity. 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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