New Data Show Near Elimination of Sickle Cell Disease-Related Vaso-Occlusive Crises and Acute Chest Syndrome with bluebird bio's LentiGlobin™ Gene Therapy for Sickle Cell Disease at 25th EHA Congress

99.5% reduction in annualised rate of vaso-occlusive crises (VOC) and acute chest syndrome (ACS) in Group C patients with history of VOCs and ACS[1]

Group C patients with at least 6 months follow-up continue to produce consistent levels of gene therapy-derived anti-sickling hemoglobin (HbA^{T87Q}) at up to 24 months[1]

Key markers of haemolysis approach near-normal levels in Groups C patients,[1] supporting the potential of LentiGlobin for sickle cell disease (*SCD) to modify the underlying pathophysiology of the disease*

ZUG, Switzerland—Jun. 12, 2020— bluebird bio, GmbH. (Nasdaq: BLUE) announced that new data from its ongoing Phase 1/2 HGB-206 study of investigational LentiGlobin™ gene therapy for adult and adolescent patients with sickle cell disease show a near-complete (99.5%) reduction of vaso-occlusive crises and acute chest syndrome. These data are being presented at the Virtual Edition of the 25th European Hematology Association (EHA25) Annual Congress.

"Vaso-occlusive crises are the painful, life-threatening episodes that are the primary clinical manifestation of SCD. The nearly complete elimination of VOCs that we saw in this study is impressive and demonstrates the potential of LentiGlobin for SCD as a treatment for this serious disease," said David Davidson, M.D., chief medical officer, bluebird bio. "These results illustrate the type of outcomes we believe are needed to provide truly meaningful improvements for people living with sickle cell disease."

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). HbS causes red blood cells (RBCs) to become sickled and fragile, resulting in chronic haemolytic anaemia, vasculopathy and unpredictable, painful VOCs.[2,3,4,5,6] For adults and children living with SCD, this can mean painful crises and other life altering or life-threatening acute complications—such as ACS, stroke and infections – and chronic end-organ complications, which can contribute to morbidity and early mortality in these patients.[5,7,8,9]

"As a treating physician of sickle cell for over 10 years, the excruciating pain crises that my patients suffer from is one of the most challenging and frustrating aspects of this disease," said presenting study author Julie Kanter, M.D., University of Alabama at Birmingham. "The promising results of this study which show patients have an almost complete elimination of VOCs and ACS, suggest LentiGlobin for SCD has real potential to provide a significant impact for people living with sickle cell disease."

LentiGlobin for SCD was designed to add functional copies of a modified form of the β-globin gene into a patient's own hematopoietic (blood) stem cells (HSCs).[10] If the treatment is successful, the patients' RBCs can produce anti-sickling haemoglobin that decreases the proportion of sickled haemoglobin, with

the goal of reducing sickled RBCs, haemolysis and other complications.[2] As of March 3, 2020, a total of 37 patients have been treated with LentiGlobin for SCD to-date in the HGB-205 and HGB-206 phase 1/2 clinical studies.

HGB-206: Group C Updated Efficacy Results

HGB-206 is an ongoing, Phase 1/2 open-label study designed to evaluate the efficacy and safety of LentiGlobin gene therapy for SCD that includes three treatment cohorts: Groups A, B and C. In Group C, 25 patients were treated with LentiGlobin for SCD gene therapy and have up to 24.8 months of follow-up (median of 12.1; min.-max. 2.8-24.8 months).[1] All patients in Group C were able to stop regular blood transfusions and remain off transfusions at three months post-treatment.

In 16 patients with six or more months of follow-up, median levels of gene therapy-derived anti-sickling haemoglobin, HbA^{T87Q} remained above 40% of total haemoglobin. At last visit in the data reported, total haemoglobin and HbA^{T87Q} levels ranged from 9.6 – 16.2 g/dL and 2.7 – 9.4 g/dL, respectively.[1]

There was a 99.5% mean reduction [95% CI, 92.4 – 100%] in the annualised rate of VOC and ACS among the 14 patients evaluated.[1] There were no reports of ACS or serious VOC at up to 24 months post-treatment in these patients. These 14 patients had a median of 8 events (4 – 28 events) in the two years prior to treatment. One non-serious Grade 2 VOC was observed in a patient approximately 3.5 months post-treatment with LentiGlobin for SCD.[1]

These results are further reinforced by the reduction in key markers of haemolysis after treatment with LentiGlobin for SCD and by findings presented from exploratory assays designed to assess the relationship between LentiGlobin for SCD and RBC physiology. The analysis in a subset of patients showed that on average the proportion of RBCs containing βA^{T87Q} from LentiGlobin-treated patients was ≥ 70% by Month 6 (n=9) and ~90% by Month 18 (n=9) post-treatment.[1] This is indicative of a pan-cellular distribution of HbA^{T87Q} believed to be critical to LentiGlobin's disease modifying effect in SCD.

HGB-206: Group C Safety Results

As of March 3, 2020, the safety data from all patients in HGB-206 are reflective of underlying SCD and the known side effects of HSC collection and myeloablative conditioning. There were no serious adverse events (SAEs) related to LentiGlobin for SCD, and the non-serious, related adverse events (AEs) were mild-to-moderate in intensity and self-limited.[1]

One patient with a history of frequent pre-treatment VOE, pulmonary hypertension, venous thrombosis, sleep apnea and asthma had complete resolution of VOEs following treatment, but suffered sudden death 20 months after LentiGlobin for SCD. The patient's autopsy revealed cardiac enlargement and fibrosis, and concluded this death was cardiovascular with contributions from asthma and SCD. The treating physician and an independent monitoring committee agreed this death was unlikely related to LentiGlobin for SCD gene therapy.[1]

About LentiGlobin for Sickle Cell Disease

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

LentiGlobin for SCD received Orphan Medicinal Product designation from the European Commission for the treatment of SCD. The U.S. Food and Drug Administration (FDA) granted Orphan Drug status, Regenerative Medicine Advanced Therapy (RMAT) designation, and Rare Pediatric Disease designation for LentiGlobin for SCD.

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

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.

For further information, visit **bluebirdbio.co.uk.**
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