Phase 3 Studies Support Maintained Transfusion Independence for Patients Across Genotypes Treated with betibeglogene autotemcel (LentiGlobin for β-thalassaemia) Gene Therapy

Northstar-2 (HGB-207) Efficacy

As of March 3, 2020, all 23 patients in HGB-207 were treated and have been followed for a median of 19.4 (min-max: 12.3 – 31.4) months.[Error! Bookmark not defined.] These patients ranged in age from four to 34 years. Only 19 patients were evaluable for TI; four additional patients do not yet have sufficient follow-up to be assessed.

89% of evaluable patients (17/19) achieved the primary endpoint of TI, with median weighted average total Hb levels of 11.9 g/dL (min-max: 9.4 – 12.9 g/dL).[Error! Bookmark not defined.] These 17 patients previously required a median of 17.5 transfusions per year (min-max: 11.5 – 37). 91% of patients (20/22) with at least 8.8 months of follow-up have stopped transfusions and total Hb was near normal in most.[Error! Bookmark not defined.]

Improved iron levels, as measured by serum ferritin and hepcidin (proteins involved in iron storage and homeostasis), were observed and trends toward improved iron management were seen. Over half of patients stopped chelation therapy, which is needed to reduce iron excess caused by chronic blood transfusions. Seven out of 23 patients began using phlebotomy for iron reduction.[Error! Bookmark not defined.]

Improvements in dyserythropoiesis, abnormal RBC production, were observed in patients with TDT who were transfusion-free and had reached 12 months of follow-up. Patients who were transfusion-free showed improved bone marrow cellularity and M:E ratio (myeloid to erythroid), indicating an improvement in bone marrow functioning and a trend toward normalisation of soluble transferrin receptor and reticulocyte counts, markers of RBC destruction. These effects demonstrate the disease-modifying potential of gene therapy for TDT for patients with this disease.[Error! Bookmark not defined.]

Northstar-3 (HGB-212) Efficacy

As of March 3, 2020, 15 patients (genotypes: nine β^0/β^0, three β^0/β+IVS1-110, three homozygous IVS-1-110 mutation) were treated and had a median follow-up of 14.4 months (min-max: 1.1–24.0 months). Median age at enrolment was 15 years of age (min-max: 4 – 33 years).[Error! Bookmark not defined.]

75% (six of eight) of evaluable patients achieved TI, with median weighted average total Hb levels of 11.5 g/dL (min-max: 9.5 – 13.5 g/dL) during TI, and continued to maintain TI for a median duration of 13.6 months (min-max: 12.2– 21.2 months) as of the data cut off.[Error! Bookmark not defined.]

85% of patients (11/13) with at least seven months of follow-up had not received a transfusion in more than seven months at time of data cutoff. These 11 patients previously required a median of 18.5 transfusions per year (min.-max.: 11.0 – 39.5 transfusions per year). In these patients, gene therapy-derived HbAT87Q supported total Hb levels ranging from 8.8–14.0 g/dL at last visit.[Error! Bookmark not defined.]

Gene therapy for β-thalassemia Safety
Non-serious adverse events (AEs) observed during the HGB-207 and HGB-212 trials that were considered related or possibly related to **gene therapy for β-thalassemia** were tachycardia, abdominal pain, pain in extremities, leukopenia, neutropenia and thrombocytopenia.[Error! Bookmark not defined.,Error! Bookmark not defined.] One serious AE (SAE) of prolonged thrombocytopenia was considered possibly related to **gene therapy for β-thalassemia**.[Error! Bookmark not defined.] In HGB-207, SAEs post-infusion in ≥2 patients included three events of veno-occlusive liver disease and two of thrombocytopaenia.[Error! Bookmark not defined.] In HGB-212, there were 8 SAEs post infusion in three patients, all events resolved.[Error! Bookmark not defined.]

Additional AEs observed in clinical studies were consistent with the known side effects of HSC mobilisation and bone marrow ablation with busulfan, including SAEs of veno-occlusive disease.[Error! Bookmark not defined.,Error! Bookmark not defined.]

In both Phase 3 studies, there have been no new unexpected safety events, no deaths, no graft failure, no cases of vector-mediated replication competent lentivirus or clonal dominance, no leukaemia and no lymphoma.[Error! Bookmark not defined.,Error! Bookmark not defined.]

About bluebird bio
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.

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References

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[2] Yannaki E et al. Betibeglogene autotemcel (LentiGlobin for β-thalassemia) in patients with transfusion-dependent β-thalassemia and β0/β0, β+IVS1-110/β+IVS1-110, or β0/β+IVS1-110 genotypes: updated results from the HGB-212 study. Poster presentation (Abstract #EP1494). 25th European Hematology Association (EHA25) Annual Congress; Virtual Congress, 11-21 June 2020.