# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 20549**

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# FORM 8-K

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**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): June 12, 2020**

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# bluebird bio, Inc.

**(Exact name of Registrant as Specified in Its Charter)**

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| **Delaware** | **001-35966** | **13-3680878** |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |

| **60 Binney Street, Cambridge, MA** | **02142** |
|---|---|
| **(Address of Principal Executive Offices)** | **(Zip Code)** |

**Registrant's Telephone Number, Including Area Code: (339) 499-9300**

**Not Applicable**
**(Former Name or Former Address, if Changed Since Last Report)**

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Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

| Title of each class | Trading Symbol(s) | Name of each exchange on which registered |
|---|---|---|
| Common Stock, $0.01 par value per share | BLUE | The NASDAQ Stock Market LLC |

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

**Item 8.01 Other Events.**

On June 12, 2020, bluebird bio, Inc. ("bluebird") issued press releases announcing updated clinical data being presented at the Virtual Edition of the 25th Congress of the European Hematology Association from the HGB-206 clinical study in sickle cell disease, and the HGB-207 and HGB-212 clinical studies in transfusion-dependent beta-thalassemia. The full text of bluebird's press releases is filed as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Press release issued by bluebird bio, Inc. on June 12, 2020. |
| 99.2 | Press release issued by bluebird bio, Inc. on June 12, 2020. |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: June 12, 2020

**bluebird bio, Inc.**

By: /s/ Jason F. Cole

Jason F. Cole

*Chief Operating and Legal Officer*

**Exhibit 99.1**

**New Data Show Near Elimination of Sickle Cell Disease-Related Vaso-Occlusive Crises and Acute Chest Syndrome in Phase 1/2 Clinical Study of bluebird bio's LentiGlobin™ Gene Therapy for Sickle Cell Disease at 25th EHA Congress**

*99.5% reduction in annualized rate of vaso-occlusive crises (VOC) and acute chest syndrome (ACS) in Group C patients with a history of VOCs and ACS (n=14) who had at least six months follow-up*

*At up to 24 months, no reports of serious VOC or ACS in Group C patients (n=18) with at least six months follow-up*

*Group C patients with at least six months follow-up continue to produce consistent levels of gene therapy-derived anti-sickling hemoglobin ($HbA^{T87Q}$) at up to 24 months, reducing levels of abnormal sickle hemoglobin (HbS)*

*Key markers of hemolysis approach near-normal levels in Group C patients, supporting the potential of LentiGlobin for SCD to modify the underlying pathophysiology of the disease*

CAMBRIDGE, Mass.— (BUSINESS WIRE) June 12, 2020 — bluebird bio, Inc. (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 (SCD) show a near-complete reduction of serious vaso-occlusive crises (VOCs) and acute chest syndrome (ACS). These data are being presented at the Virtual Edition of the 25th European Hematology Association (EHA25) Annual Congress.

"Vaso-occlusive crises (VOCs) are the painful, life-threatening episodes that are the primary clinical manifestation of sickle cell disease. 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. In addition, the improvement of laboratory measures of hemolysis and red cell physiology, with nearly pan-cellular distribution of the anti-sickling $HbA^{T87Q}$, suggest LentiGlobin for SCD may substantially modify the causative pathophysiology of SCD. We are pleased to have reached a general agreement with the FDA on the clinical data required to support a submission for LentiGlobin for SCD and we plan to seek an accelerated approval. We look forward to working with the entire SCD community to bring forward a disease modifying option for patients."

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 hemoglobin (HbS). HbS causes red blood cells to become sickled and fragile, resulting in chronic hemolytic anemia, vasculopathy and unpredictable, painful VOCs. For adults and children living with SCD, this means painful crises and other life altering or life-threatening acute complications—such as ACS, stroke and infections. If patients survive the acute complications, vasculopathy and end-organ damage, resulting complications can lead to pulmonary hypertension, renal failure and early death; in the U.S. the median age of death for someone with sickle cell disease is 43 - 46 years.

"As a physician treating 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 ($\beta^{A\text{-}T87Q}$-globin gene) into a patient’s own hematopoietic (blood) stem cells (HSCs). Once patients have the $\beta^{A\text{-}T87Q}$-globin gene, their red blood cells can produce anti-sickling hemoglobin, $HbA^{T87Q}$, that decreases the proportion of HbS, with the goal of reducing sickled red blood cells, hemolysis and other complications.
As of March 3, 2020, a total of 37 patients have been treated with LentiGlobin for SCD to-date in the HGB-205 (n=3) and HGB-206 (n=34) clinical studies. The HGB-206 total includes: Group A (n=7), B (n=2) and C (n=25).

**HGB-206: Group C Updated Efficacy Results**
In Group C of HGB-206, 25 patients were treated with LentiGlobin for SCD and have up to 24.8 months of follow-up (median of 12.1; min.-max.: 2.8—24.8 months). Results from Group C are as of March 3, 2020 and include efficacy data for 16 patients who had at least a Month 6 visit, and safety data for 18 patients, which includes two patients who were at least six months post-treatment but results from a Month 6 visit are not available.

In 16 patients with six or more months of follow-up, median levels of gene therapy-derived anti-sickling hemoglobin, $HbA^{T87Q}$, were maintained with $HbA^{T87Q}$ contributing at least 40% of total hemoglobin. At last visit reported, total hemoglobin ranged from 9.6 – 16.2 g/dL and $HbA^{T87Q}$ levels ranged from 2.7 – 9.4 g/dL. At Month 6 the production of $HbA^{T87Q}$ was associated with a reduction in the proportion of HbS in total hemoglobin. Patients had a median of ≤ 60% HbS. All patients in Group C were able to stop regular blood transfusions and remain off transfusions at three months post-treatment.

There was a 99.5% mean reduction in annualized rate of VOC and ACS among the 14 patients who had at least six months of follow-up and a history of VOCs or ACS, defined as four or more VOC or ACS events in the two years prior to treatment. These 14 patients had a median of eight events in the two years prior to treatment (min.-max.: 4 – 28 events).

There were no reports of serious VOCs or ACS at up to 24 months post-treatment in patients with at least six months of follow-up (n=18). As previously reported, one non-serious Grade 2 VOC was observed in a patient approximately 3.5 months post-treatment with LentiGlobin for SCD.

In sickle cell disease, red blood cells become sickled and fragile, rupturing more easily than healthy red blood cells. The breakdown of red blood cells is hemolysis and this process occurs normally in the body. However, in sickle cell disease hemolysis happens too quickly due to the fragility of the red blood cells, which results in hemolytic anemia.

Patients treated with LentiGlobin for SCD demonstrated improvement in key markers of hemolysis, which are indicators of the health of red blood cells. Lab results assessing these indicators were available for the majority of the 18 patients with ≥ 6 months of follow-up. The medians for reticulocyte counts (n=15), lactate dehydrogenase (LDH) levels (n=13) and total bilirubin (n=16) improved compared to screening and stabilized by Month 6. In patients with Month 24 data (n=5)

these values approached the upper limit of normal by Month 24. These results suggest treatment with LentiGlobin for SCD is improving biological markers of sickle cell disease.

Assays were developed by bluebird bio to enable the detection of $HbA^{T87Q}$ and HbS protein in individual red blood cells as well as to assess if $HbA^{T87Q}$ was pancellular, present throughout all of a patient's red blood cells. Samples from a subset of patients in Group C were assessed. In nine patients who had at least six months of follow-up, the average proportion of red blood cells positive for $HbA^{T87Q}$ was greater than 70%, and on average more than 85% of red blood cells contained $HbA^{T87Q}$ at 18 months post-treatment, suggesting near-complete pancellularity of $HbA^{T87Q}$ distribution.

**HGB-206: Group C Safety Results**
As of March 3, 2020, the safety data from all patients in HGB-206 are generally reflective of underlying SCD and the known side effects of hematopoietic stem cell collection and myeloablative conditioning. There were no serious adverse events related to LentiGlobin for SCD, and the non-serious, related adverse events (AEs) were mild-to-moderate in intensity and self-limited.

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

The presentation is now available on demand on the EHA25 website:

- **Abstract #S282:** "Outcomes in patients treated with LentiGlobin for sickle cell disease (SCD) gene therapy: Updated results from the Phase 1/2 HGB-206 group C study"

**About HGB-206**
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 (n=7), B (n=2) and C (n=25). A refined manufacturing process that was designed to increase vector copy number (VCN) and improve engraftment potential of gene-modified stem cells was 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.

**LentiGlobin for Sickle Cell Disease Regulatory Status**
bluebird bio reached general agreement with the U.S. Food and Drug Administration (FDA) that the clinical data package required to support a Biologics Licensing Application (BLA) submission for LentiGlobin for SCD will be based on data from a portion of patients in the HGB-206 study Group C that have already been treated. The planned submission will be based on an analysis using complete resolution of severe vaso-occlusive events (VOEs) as the primary endpoint with at least 18 months of follow-up post-treatment with LentiGlobin for SCD. Globin response will be used as a key secondary endpoint.

bluebird bio anticipates additional guidance from the FDA regarding the commercial manufacturing process, including suspension lentiviral vector. bluebird bio announced in a May 11, 2020 press

release it plans to seek an accelerated approval and expects to submit the U.S. BLA for SCD in the second half of 2021.

**About LentiGlobin for Sickle Cell Disease**
LentiGlobin for sickle cell disease 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. FDA granted orphan drug designation, 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.

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 betibeglogene autotemcel for β-thalassemia or LentiGlobin for SCD. For more information visit: https://www.bluebirdbio.com/our-science/clinical-trials or clinicaltrials.gov and use identifier NCT02633943 for LTF-303.

**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-thalassemia 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., and Zug, Switzerland. For more information, visit bluebirdbio.com.

Follow bluebird bio on social media: @bluebirdbio, LinkedIn, Instagram and YouTube.



**bluebird bio 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 development and regulatory plans for the LentiGlobin for SCD product candidate, and the company's intentions regarding the timing for providing further updates on the development of the product candidate. 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 COVID-19 pandemic and resulting impact on our operations and healthcare systems will affect the execution of our development plans*

*or the conduct of our clinical studies; the risk that even if LentiGlobin for SCD addresses ACS and VOC events, that it may not address progressive organ damage experienced by patients with SCD; the risk that the efficacy and safety results observed in the patients treated in our prior and ongoing clinical trials of LentiGlobin for SCD may not persist or be durable; the risk that the efficacy and safety results from our prior and ongoing clinical trials will not continue or be repeated in when treating additional patients in our ongoing or planned clinical trials; the risk that the HGB-206 and HGB-210 clinical studies as currently contemplated may be insufficient to support regulatory submissions or marketing approval in the United States and European Union; the risk that regulatory authorities will require additional information regarding our product candidate, resulting in a delay to our anticipated timelines for regulatory submissions, including our application for marketing 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-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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# # #

**Exhibit 99.2**

**Majority of Evaluable Patients Across Genotypes Achieve Transfusion Independence and Maintain It with Near-Normal Hemoglobin Levels in Phase 3 Studies of betibeglogene autotemcel (LentiGlobin™ for β-thalassemia) Gene Therapy Presented at 25th EHA Congress**

*89% of evaluable patients (17/19) with transfusion-dependent β-thalassemia who do not have a $\beta^0/\beta^0$ genotype achieved transfusion independence with 11.9 g/dL median weighted average total hemoglobin (Hb) level in HGB-207*

*Data from exploratory analyses of HGB-207 show improved markers of blood cell production and bone marrow function in patients who achieved transfusion independence*

*85% of patients (11/13) with a β0/β0 genotype or IVS-I-110 mutation in HGB-212 have been transfusion-free for at least 7 months*

CAMBRIDGE, Mass.— (BUSINESS WIRE) June 12, 2020 – bluebird bio, Inc. (Nasdaq: BLUE) today announced that new data from ongoing Phase 3 studies of betibeglogene autotemcel (beti-cel; formerly LentiGlobin™ for β-thalassemia gene therapy) show pediatric, adolescent and adult patients with a range of genotypes of transfusion-dependent β-thalassemia (TDT) achieve and maintain transfusion independence with hemoglobin (Hb) levels that are near-normal (≥10.5 g/dL). These data are being presented at the Virtual Edition of the 25th European Hematology Association (EHA25) Annual Congress.

“With more than a decade of clinical experience evaluating gene therapy in patients with transfusion dependent β-thalassemia across a wide range of ages and genotypes, we have built the most comprehensive understanding of treatment outcomes in the field,” said David Davidson, M.D., chief medical officer, bluebird bio. “Seeing patients achieve transfusion independence and maintain that positive clinical benefit over time with robust hemoglobin levels reflects our initial vision of the potential of beti-cel. The accumulating long-term data demonstrating improvements in bone marrow histology, iron balance and red cell biology support the potential of beti-cel to correct the underlying pathophysiology of transfusion-dependent β-thalassemia.”

A total of 60 pediatric, adolescent and adult patients across genotypes of TDT have been treated with beti-cel in the Phase 1/2 Northstar (HGB-204) and HGB-205 studies, and the Phase 3 Northstar-2 (HGB-207) and Northstar-3 (HGB-212) studies as of March 3, 2020. In studies of beti-cel, transfusion independence 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.

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

“Patients with transfusion-dependent β-thalassemia do not make enough healthy red blood cells and cannot live without chronic transfusions; for patients that means a lifetime of necessary visits to a hospital or clinic and reliance on an often unreliable blood supply, which compounds the challenges of managing this disease,” said presenting study author Professor John B. Porter, MA, M.D., FRCP, FRCPath, University College London Hospital, London, UK. “These results showing

patients free from transfusions and maintaining near-normal hemoglobin levels after treatment with beti-cel is a positive outcome for people living with transfusion-dependent β-thalassemia. In addition, we now have more data that provide further evidence that most of these patients have a measurable improvement in markers of healthy red blood cell production."

Beti-cel is a one-time gene therapy designed to address the underlying genetic cause of TDT by adding 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). This means there is no need for donor HSCs from another person, as is required for allogeneic HSC transplantation (allo-HSCT). Once a patient has the $\beta^{A\text{-}T87Q}$-globin gene, they have the potential to produce $HbA^{T87Q}$, which is gene therapy-derived Hb, at levels that eliminate or significantly reduce the need for transfusions.

**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 months. These patients ranged in age from four to 34 years, including eight pediatric (<12 years of age) and 15 adolescent/adult (≥12 years of age) patients. Only 19 patients were evaluable for transfusion independence; four additional patients do not yet have sufficient follow-up to be assessed for transfusion independence.

Eighty-nine percent of evaluable patients (17/19) achieved transfusion independence, with median weighted average total Hb levels of 11.9 g/dL (min-max: 9.4 – 12.9 g/dL) over a median of 19.4 months of follow-up to date (min-max: 12.3 – 31.4 months). These 17 patients previously required a median of 17.5 transfusions per year (min-max: 11.5 – 37 transfusions per year).

Improved iron levels, as measured by serum ferritin and hepcidin levels (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 excess iron caused by chronic blood transfusions. Seven out of 23 patients began using phlebotomy for iron reduction.

**Analysis of Healthy Red Blood Cell Production**
In exploratory analyses, biomarkers of ineffective erythropoiesis (red blood cell production) were evaluated in patients who achieved transfusion independence in HGB-207.

The myeloid to erythroid (M:E) ratio in bone marrow from patients who achieved transfusion independence increased from a median of 1:3 (n=17) at baseline to 1:1.2 (n=16) at Month 12. Improvement of the M:E ratio, the ratio of white blood cell and red blood cell precursors in the bone marrow, suggests an improvement in mature red blood cell production. Images illustrating the bone marrow cellularity at baseline, Month 12 and Month 24 are available in the EHA25 presentation (abstract #S296): "Improvement in erythropoiesis in patients with transfusion-dependent β-thalassemia following treatment with betibeglogene autotemcel (LentiGlobin for β-thalassemia) in the Phase 3 HGB-207 study".

Additionally, biomarkers of erythropoiesis continue to demonstrate a trend toward normalization in patients who achieved transfusion independence, including improved levels over time of erythropoietin, a hormone involved in red blood cell production; reticulocytes, immature red blood cells; and soluble transferrin receptor, a protein measured to help evaluate iron status. The continued normalization of red blood cell production over time among some patients who achieved transfusion independence supports the disease-modifying potential of beti-cel in patients with TDT.

**Northstar-3 (HGB-212) Efficacy**
As of March 3, 2020, 15 patients (genotypes: 9 $\beta^0/\beta^0$, 3 $\beta^0$/ β+IVS1-110, 3 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 enrollment was 15 (min-max: 4 – 33 years).

Six of eight evaluable patients achieved transfusion independence, with median weighted average total Hb levels of 11.5 g/dL (min-max: 9.5 – 13.5 g/dL), and continued to maintain transfusion independence for a median duration of 13.6 months (min-max: 12.2– 21.2 months) as of the data cutoff.

Eighty-five percent 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 $HbA^{T87Q}$ supported total Hb levels ranging from 8.8–14.0 g/dL at last visit.

**Betibeglogene autotemcel Safety**
Non-serious adverse events (AEs) observed during the HGB-207 and HGB-212 trials that were considered related or possibly related to beti-cel were tachycardia, abdominal pain, pain in extremities, leukopenia, neutropenia and thrombocytopenia. One serious event of thrombocytopenia was considered possibly related to beti-cel.

In HGB-207, serious events post-infusion in ≥ two patients included three events of veno-occlusive liver disease and two events of thrombocytopenia. In HGB-212, serious events post-infusion in ≥ two patients included two events of pyrexia.

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.

In both Phase 3 studies, there have been no deaths, no graft failure, no cases of vector-mediated replication competent lentivirus or clonal dominance, no leukemia and no lymphoma.

The presentations are now available on demand on the EHA25 website:

- **Abstract #S296**: “Improvement in erythropoiesis in patients with transfusion-dependent β-thalassemia following treatment with betibeglogene autotemcel (LentiGlobin for β-thalassemia) in the Phase 3 HGB-207 study.”

- **Abstract #EP1494:** “Betibeglogene autotemcel (LentiGlobin) in patients with transfusion-dependent β-thalassemia and β0/β0, β+IVS-I-110/β+IVS-I-110, or β0/β+IVS-I-110 genotypes: Updated results from the HGB-212 study.”

**About betibeglogene autotemcel**
The European Commission granted conditional marketing authorization (CMA) for betibeglogene autotemcel (beti-cel; formerly LentiGlobin™ gene therapy for β-thalassemia), marketed as ZYNTEGLO™ gene therapy, for patients 12 years and older with transfusion-dependent β-thalassemia (TDT) who do not have a $\beta^0/\beta^0$ genotype, for whom hematopoietic stem cell (HSC) transplantation is appropriate, but a human leukocyte antigen (HLA)-matched related HSC donor is not available. On April 28, 2020, the European Medicines Agency (EMA) renewed the CMA for

ZYNTEGLO, supported by data from 32 patients treated with ZYNTEGLO, including three patients with up to five years of follow-up.

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

Beti-cel 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 hemoglobin, at levels that may eliminate or significantly reduce the need for transfusions.

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 and non-cardiac chest pain. Two serious adverse events (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.

The CMA for beti-cel is valid in the 27 member states of the EU as well as UK, Iceland, Liechtenstein and Norway. For details, please see the Summary of Product Characteristics (SmPC).

The U.S. Food and Drug Administration (FDA) granted beti-cel orphan drug designation and Breakthrough Therapy designation for the treatment of transfusion-dependent β-thalassemia. Beti-cel is not approved in the U.S.

Beti-cel continues to be evaluated in the ongoing Phase 3 Northstar-2 and Northstar-3 studies. For more information about the ongoing clinical studies, visit www.northstarclinicalstudies.com or clinicaltrials.gov and use identifier NCT02906202 for Northstar-2 (HGB-207) and 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 betibeglogene autotemcel or LentiGlobin for SCD. For more information visit: https://www.bluebirdbio.com/our-science/clinical-trials or clinicaltrials.gov and use identifier NCT02633943 for LTF-303.

**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-thalassemia 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.; and Zug, Switzerland. For more information, visit bluebirdbio.com.

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**bluebird bio Forward-Looking Statements**
*This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. 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 COVID-19 pandemic and resulting impact on our operations and healthcare systems will affect the execution of our development plans or the conduct of our clinical studies; the risk that the efficacy and safety results observed in the patients treated in our prior and ongoing clinical trials of beti-cel may not persist; and the risk that the efficacy and safety results from our prior and ongoing clinical trials will not continue or be repeated with additional patients in our ongoing or planned clinical trials or in the commercial context; the risk that the FDA will require additional information regarding beti-cel, resulting in a delay to our anticipated timelines for regulatory submissions, including submission of our BLA. 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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