

---

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

---

**FORM 8-K**

---

**CURRENT REPORT**  
**Pursuant to Section 13 or 15(d) of The Securities Exchange Act of 1934**

**Date of Report (Date of Earliest Event Reported): December 3, 2016**

---

**bluebird bio, Inc.**

(Exact name of registrant as specified in its charter)

---

---

**DELAWARE**

(State or other jurisdiction of  
incorporation)

---

**001-35966**

(Commission File Number)

---

**13-3680878**

(I.R.S. Employer  
Identification No.)

---

**150 Second Street  
Cambridge, MA**

(Address of principal executive offices)

---

**02141**

(Zip Code)

Registrant's telephone number, including area code **(339) 499-9300**

Not Applicable

(Former name or former address, if changed since last report)

---

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:

- 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))
- 
-

**Item 8.01 Other Events**

On December 3, 2016, bluebird bio, Inc. (“bluebird”) issued a press release announcing clinical data from its HGB-205 study of the LentiGlobin product candidate, presented at the 58<sup>th</sup> Annual Meeting of the American Society of Hematology (“ASH”) on December 3, 2016. The full text of the press release regarding the announcement is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

On December 5, 2016, bluebird issued a press release announcing clinical data from its Northstar (HGB-204) and HGB-206 studies of its LentiGlobin product candidate presented at ASH on December 5, 2016, and of clinical development plans for its Lenti-D product candidate. The full text of the press release regarding this announcement is filed as Exhibit 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 December 3, 2016
99.2	Press release issued by bluebird bio, Inc. on December 5, 2016

---

**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: December 5, 2016

**bluebird bio, Inc.**

By: /s/ Jason F. Cole

\_\_\_\_\_  
Jason F. Cole

*Chief Legal Officer*

---

## EXHIBIT INDEX

Exhibit No.	Description
99.1	Press release issued by bluebird bio, Inc. on December 3, 2016
99.2	Press release issued by bluebird bio, Inc. on December 5, 2016

**bluebird bio Presents New Data from HGB-205 Study of LentiGlobin™ Drug Product in Patients with Transfusion-Dependent  $\beta$ -Thalassemia (TDT) and Severe Sickle Cell Disease at American Society of Hematology (ASH) Annual Meeting**

*-First patient with severe sickle cell disease treated with gene therapy remains free of clinical symptoms 21 months after receiving LentiGlobin Drug Product –*

*-Ongoing transfusion independence and sustained production of HbA<sup>T87Q</sup> in patients with transfusion-dependent  $\beta$ -thalassemia –*

*-Company to host event at ASH with live webcast, Monday, December 5 at 8:30 p.m. PT –*

**San Diego, CA, December 3, 2016** – bluebird bio, Inc. ([Nasdaq: BLUE](#)), a clinical-stage company committed to developing potentially transformative gene therapies for severe genetic diseases and T cell-based immunotherapies for cancer, announced the presentation of new data from the ongoing HGB-205 clinical study evaluating its LentiGlobin product candidate in patients with transfusion-dependent  $\beta$ -thalassemia (TDT) and severe sickle cell disease (SCD) at the 58th American Society of Hematology Annual Meeting.

The data from the HGB-205 study were highlighted today in a poster presentation by Marina Cavazzana, M.D., Ph.D., lead investigator of the HGB-205 study conducted in Necker Hospital, AP-HP and professor of hematology at Paris Descartes University, head of the department of Biotherapy Hospital, the clinical research center of Biotherapy at Necker Enfants Malades - Greater Paris University Hospitals, AP-HP and Inserm) and the Lymphohematopoiesis Laboratory, Institute of Genetic Diseases, Imagine, Paris, France.

“We believe the enduring responses seen in this study - in the patients with TDT as well as the patient with SCD - demonstrate the continued promise of LentiGlobin gene therapy in both of these patient populations. We have seen nearly three years of transfusion independence in TDT in certain patients, providing important data on the long-term safety and durability of this therapy,” said David Davidson, M.D., chief medical officer, bluebird bio. “In addition, it is encouraging that the patient with SCD has remained free of acute SCD-related clinical events in the 21 months since treatment, when he previously required monthly blood transfusions to help control his SCD symptoms. This patient’s successful outcome not only offers hope for the potential of LentiGlobin to benefit other patients with SCD, but also provides important insights into this complex disease that we are applying to our ongoing HGB-206 study.”

## Abstract #2311: Update from the HGB-205 Phase 1/2 Clinical Study of LentiGlobin Gene Therapy: Sustained Clinical Benefit in Severe Hemoglobinopathies

HGB-205 is an ongoing, open-label, single-center Phase 1/2 study designed to evaluate the safety and efficacy of LentiGlobin drug product in the treatment of patients with TDT and severe SCD. Four patients with TDT and one patient with severe SCD have undergone infusion with LentiGlobin drug product in this study as of September 9, 2016. The patients with TDT have between 11.6 and 33.5 months of follow-up, and the patient with SCD has 22.9 months of follow-up.

### Key Results as of September 9, 2016 Data Cut-off:

- Three patients with TDT and  $\beta^0/\beta^E$  genotype have remained free of transfusions since shortly after receiving LentiGlobin treatment. Patient 1201 has been free of transfusions for 33.1 months with total hemoglobin of 10.9 g/dL, of which 7.7 g/dL was HbAT87Q. Patient 1202 has been free of transfusions for 29.9 months with total hemoglobin of 13.5 g/dL, of which 10.1 g/dL was HbAT87Q. In addition, this patient has been able to stop iron chelation. Patient 1206 has been free of transfusions for 11.5 months with total hemoglobin of 11.3 g/dL, of which 8.6 g/dL was HbAT87Q.
- Patient 1203 with TDT and homozygosity for the severe  $\beta^+$  mutation IVS1-110 has been free of transfusions for 11.6 months (since approximately 3 months after receiving LentiGlobin treatment) with total hemoglobin of 8.3 g/dL, of which 6.7 g/dL was HbAT87Q.
- Patient 1204 with severe SCD at 21-month post-drug infusion was producing 48% HbAT87Q – well above the 30 percent threshold of anti-sickling Hb that may potentially achieve a disease-modifying clinical effect.
- Prior to drug product infusion, Patient 1204 required monthly blood transfusions after failure of hydroxyurea treatment to help control his SCD symptoms; he has not received RBC transfusions since shortly after LentiGlobin infusion. Since infusion, this patient has had no hospitalizations or acute SCD-related events.
- No LentiGlobin-related adverse events have been observed for the patients with either TDT or SCD; the adverse events observed are generally consistent with myeloablative conditioning.
- All five treated patients successfully engrafted and insertional site analyses demonstrate highly polyclonal reconstitution without clonal dominance.

“These data show a stable clinical and biological effect in patients with TDT or severe SCD who have received a one-time treatment with LentiGlobin,” said Professor Cavazzana. “We are now seeing the benefit of gene therapy with LentiGlobin beyond two years in TDT in certain patients, and clinical benefit continues to be realized in the patient with severe SCD after almost 24 months of follow-up. We are encouraged by



these results and the potential benefit treatment with LentiGlobin can have on patients living with these debilitating diseases and without an HLA compatible sibling donor.”

#### **Webcast Information**

bluebird bio will host a live webcast at 8:30 p.m. PT (11:30 p.m. ET) on Monday, December 5, 2016. The live webcast can be accessed under "Calendar of Events" in the Investors and Media section of the company's website at [www.bluebirdbio.com](http://www.bluebirdbio.com).

#### **About bluebird bio, Inc.**

With its lentiviral-based gene therapies, T cell immunotherapy expertise and gene editing capabilities, bluebird bio has built an integrated product platform with broad potential application to severe genetic diseases and cancer. bluebird bio’s gene therapy clinical programs include its Lenti-D™ product candidate, currently in a Phase 2/3 study, called the Starbeam Study, for the treatment of cerebral adrenoleukodystrophy, and its LentiGlobin™ BB305 product candidate, currently in four clinical studies for the treatment of transfusion-dependent  $\beta$ -thalassemia and severe sickle cell disease. bluebird bio’s oncology pipeline is built upon the company’s leadership in lentiviral gene delivery and T cell engineering, with a focus on developing novel T cell-based immunotherapies, including chimeric antigen receptor (CAR T) and T cell receptor (TCR) therapies. bluebird bio’s lead oncology program, bb2121, is an anti-BCMA CAR T program partnered with Celgene. bb2121 is currently being studied in a Phase 1 trial for the treatment of relapsed/refractory multiple myeloma. bluebird bio also has discovery research programs utilizing megaTALs/homing endonuclease gene editing technologies with the potential for use across the company’s pipeline.

bluebird bio has operations in Cambridge, Massachusetts; Seattle, Washington; 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 research, development, manufacturing and regulatory approval plans for its LentiGlobin product candidate to treat transfusion-dependent  $\beta$ -thalassemia and severe sickle cell disease. 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, risks that the preliminary positive results from our prior and ongoing clinical trials of LentiGlobin, including HGB-205, will not continue or be repeated in our ongoing or planned clinical trials of LentiGlobin, the risks that the changes we have made in the LentiGlobin manufacturing process or the HGB-206 clinical trial protocol will not result in improved patient outcomes, risks that the current or planned clinical trials of LentiGlobin will be insufficient to support regulatory submissions or marketing approval in the US and EU, the risk of a delay in the enrollment of patients in our clinical studies, and the risk that any one or more of our product candidates will not be successfully developed, approved or commercialized. 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 quarterly report on 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.*

**Contact:**

Investors:

bluebird bio, Inc.

Manisha Pai, 617-245-2107

[mpai@bluebirdbio.com](mailto:mpai@bluebirdbio.com)

Media:

bluebird bio, Inc.

Elizabeth Pingpank, 617-914-8736

[epingpank@bluebirdbio.com](mailto:epingpank@bluebirdbio.com)

or

Pure Communications, Inc.

Dan Budwick, 973-271-6085





**About AP-HP:** AP-HP - Greater Paris University hospitals - is a European world-renowned European university hospital. Its 39 hospitals treat 8 million people every year: in consultation, emergency, during scheduled or home hospitalizations. The AP-HP provides a public health service for everyone, 24 hours a day. This mission is a duty as well as a great source of pride. The AP-HP is the leading employer in the Greater Paris area : 100 000 staff members – doctors, researchers, paramedical staff, administrative personnel and workers – work there. <http://www.aphp.fr>

**About the Imagine Institute:** As the leading European center for research, care and teaching in genetic diseases, the Imagine Institute's primary aim is to understand and cure. The Institute's staff includes 850 of the best physicians, scientists and healthcare professionals housed in an innovative new building designed to realize synergies. This unprecedented continuum of expertise available in close proximity to patients allows Imagine to accelerate discoveries and their application at the bedside. [www.institutimagine.org](http://www.institutimagine.org)

#### Press contacts

**AP-HP:** Anne-Cécile Bard and Marine Leroy: +33 (0)1 40 27 37 22 - [service.presse@aphp.fr](mailto:service.presse@aphp.fr)

**Imagine:** Béatrice Parinello-Froment – [beatriceparrinello@bpfconseil.com](mailto:beatriceparrinello@bpfconseil.com) – +33 (0)6 63 72 16 06  
Clémence Inglard – [clemence.inglard@institutimagine.org](mailto:clemence.inglard@institutimagine.org) – +33 (0)1 42 75 46 44



**bluebird bio Provides Updates on HSC Gene Therapy Programs**

*-LentiGlobin™ drug product manufactured with process 2 for two patients in HGB-206 and HGB-207 confirms two-to-threefold increase in vector copy numbers (VCNs) observed in retrospective in vitro analyses of patients' transduced cells –  
-Company to host event at ASH with live webcast, Monday, December 5 at 8:30 p.m. PT –*

**San Diego, CA, December 5, 2016** – bluebird bio, Inc. ([Nasdaq: BLUE](#)), a clinical-stage company committed to developing potentially transformative gene therapies for severe genetic diseases and T cell-based immunotherapies for cancer, provided updates across its hematopoietic stem cell (HSC) gene therapy programs, including:

- Updated interim clinical data from the Northstar (HGB-204) study of LentiGlobin drug product in transfusion-dependent  $\beta$ -thalassemia (TDT) confirm patients with non- $\beta^0/\beta^0$  genotypes and  $\geq 12$  months of follow-up have stopped regular transfusions; patients with  $\beta^0/\beta^0$  genotypes and  $\geq 12$  months of follow-up had a median reduction in transfusion volume of 63%
- Drug product vector copy numbers (DP VCNs) for the first HGB-207 and HGB-206 patients who will be treated using LentiGlobin drug product made using our improved manufacturing process (process 2) are 2.9 and 3.3, respectively
- Updated interim clinical data from seven subjects in the HGB-206 study of LentiGlobin drug product in severe sickle cell disease (SCD) underscore the need for recently implemented protocol amendments seeking to improve HbA<sup>T87Q</sup> production in this population
- Company to expand enrollment in Starbeam study of Lenti-D™ in cerebral adrenoleukodystrophy (CALD) by eight patients

“Our focus is learning, adjusting and implementing to innovate on behalf of the patients we aim to serve. This year we have made tremendous progress against this objective,” said Nick Leschly, chief bluebird. “In 2016, we focused on further enhancing our LentiGlobin programs in TDT and SCD by implementing high potential manufacturing and protocol amendments while advancing our lead bb2121 oncology program and commercialization capabilities. We are encouraged by the data presented at ASH and how that has informed our plans for 2017.”

**TDT Program Updates**

The company announced that the first patient has been enrolled in Northstar-2 (HGB-207), a Phase 3, global, multi-center study in patients with TDT with non- $\beta^0/\beta^0$  genotypes. This study uses LentiGlobin drug product manufactured with updated

---



processes using transduction enhancers. LentiGlobin DP VCN for the first patient to be treated in Northstar-2 is 2.9 vector copies per diploid genome (c/dg), with 77% of the stem cells lentiviral vector positive (LVV+).

Interim data from the Northstar study were highlighted today in an oral presentation by Alexis Thompson, M.D., M.P.H., head of the hematology section of the Division of Hematology Oncology Transplantation and Director of the Comprehensive Thalassemia Program at the Ann and Robert H. Lurie Children's Hospital of Chicago, where she also serves as the A. Watson and Sarah Armour Endowed Chair for Childhood Cancer and Blood Disorders.

### **LentiGlobin Gene Therapy for Transfusion-Dependent $\beta$ -Thalassemia: Update from the Northstar (HGB-204) Phase 1/2 Clinical Study (Abstract #1175)**

The Northstar Study is an ongoing, open-label, single-dose, international, multicenter Phase 1/2 study designed to evaluate the safety and efficacy of LentiGlobin drug product for the treatment of subjects with TDT. Results as of September 16, 2016 include:

- Ten patients with non- $\beta^0/\beta^0$  genotypes and eight patients with  $\beta^0/\beta^0$  genotypes have received LentiGlobin drug product. The median follow-up was 17 months (range: 6.3 – 29.8 months); two patients have completed the two-year primary analysis period.
  - The median DP VCN for patients with non- $\beta^0/\beta^0$  genotypes was 0.8 c/dg (range: 0.3 – 1.1 c/dg); for patients with  $\beta^0/\beta^0$  genotypes, the median DP VCN was 0.7 c/dg (range: 0.3 – 1.5 c/dg). The median cell dose for patients with non- $\beta^0/\beta^0$  genotypes was  $7.1 \times 10^6$  CD34+ cells/kg (range: 5.2 –  $13.0 \times 10^6$  cells/kg); for patients with  $\beta^0/\beta^0$  genotypes, the median cell dose was  $11.0 \times 10^6$  CD34+ cells/kg (range: 6.1 –  $18.1 \times 10^6$  cells/kg).
  - The median *in vivo* VCN at six months of follow-up was 0.4 c/dg (range 0.1-0.9 c/dg, n=10) in patients with non- $\beta^0/\beta^0$  genotypes and 0.3 c/dg (range 0.1-1.0 c/dg, n=8) in patients with  $\beta^0/\beta^0$  genotypes.
  - All patients with non- $\beta^0/\beta^0$  genotypes with  $\geq 12$  months of follow-up (n=5) have stopped regular transfusions (median total hemoglobin: 11.7 g/dL; range: 9.5 – 12.5 g/dL). At last follow-up, the median total hemoglobin of all patients (n=10) with non- $\beta^0/\beta^0$  genotypes (median follow up: 14.7 months; range: 6.3 – 29.8 months) was 10.3 g/dL (range: 7.2 – 12.5 g/dl).
  - Patients with  $\beta^0/\beta^0$  genotypes and  $\geq 12$  months of follow-up had a median reduction in annualized transfusion volume of 63% (range 47 – 78%) and median reduction in annualized transfusion frequency of 65% (range 31 – 81%), calculated based on their transfusion requirements from month 6 to data cut-off. The median follow-up was 17.3 months (range: 6.7 – 25.4 months). Hemoglobin fractions at month 12 show consistent production of HbA<sup>T87Q</sup> across genotypes  $\geq 12$  months of follow-up.
  - A correlation between VCN and HbA<sup>T87Q</sup> production was observed.
-



- The safety profile remains consistent with myeloablative conditioning using single agent busulfan with no  $\geq$  Grade 3 drug product-related adverse events (AEs) reported.

“The maturing interim data from the Northstar study support the potential for LentiGlobin to provide a transformative treatment option for patients with TDT by reducing or eliminating the burdensome cycle of chronic blood transfusions and iron chelation,” said David Davidson, chief medical officer, bluebird bio. “In addition, we are pleased by the robust vector copy number and high proportion of LVV+ CD34+ stem cells in the drug product manufactured using transduction enhancers for the first patient to be treated in the Phase 3 Northstar-2 study. If the clinical correlation between drug product VCN and hemoglobin production observed in the Northstar study continues with drug product manufactured utilizing process 2, we are hopeful that LentiGlobin drug product with higher VCNs will consistently yield clinically meaningful outcomes for patients with TDT across all genotypes.”

#### **Severe Sickle Cell Disease Program Updates**

bluebird bio has amended the protocol of the ongoing HGB-206 study in patients with severe SCD to incorporate several changes with the goal of increasing production of HbA<sup>T87Q</sup>, such as increasing the percentage of transduced cells through manufacturing improvements, increasing target busulfan area under the curve (AUC), introducing a minimum period of regular blood transfusions prior to stem cell collection and exploring an alternate hematopoietic stem cell procurement method with the goal of increasing transduced cell dose. Enrollment has begun under this modified protocol, and the DP VCN for the first patient enrolled under the new protocol was 3.3 c/dg, with 83% of the stem cells LVV+, with infusion planned for early 2017.

Interim data from the HGB-206 study were highlighted today in an oral presentation by Julie Kanter, M.D., Medical University of South Carolina, Charleston, SC.

#### **Interim Results from a Phase 1/2 Clinical Study of LentiGlobin™ Gene Therapy for Severe Sickle Cell Disease (Abstract #1176)**

HGB-206 is an ongoing, open-label study designed to evaluate the safety and efficacy of LentiGlobin drug product in the treatment of subjects with severe SCD. Results, as of November 9, 2016, include:

- Seven patients with severe SCD have been infused with LentiGlobin drug product under the original study protocol. All patients are 18+ years of age with a history of symptomatic SCD, adequate organ function/performance status and no previous hematopoietic stem cell transplant or gene therapy.
  - The median LentiGlobin drug product cell dose was  $2.1 \times 10^6$  CD34+ cells/kg (range:  $1.6 - 5.1 \times 10^6$  cells/kg)
  - The median LentiGlobin DP VCN was 0.6 c/dg (range:  $0.3 - 1.3$  c/dg)
-



- The median VCN in peripheral blood at last measurement was 0.09 c/dg (range: 0.05 to 0.24 c/dg)
- Patient 1309 has seen a steady increase in hemoglobin levels and is producing 2.0 g/dL HbAT87Q with 22.8% overall anti-sickling Hb (HbAT87Q + HbF) even after a substantial drop in VCN between DP and peripheral blood at latest follow up (0.9 to 0.24 at nine months follow up). As of the data cutoff, this was the only patient in HGB-206 who received chronic transfusions prior to receiving LentiGlobin drug product.
- At last follow up, all treated patients were producing measureable HbAT87Q, with a range of 0.1 – 2.0 g/dL HbAT87Q at last follow-up. Median follow up: 11.5 months (range: 8.1 – 17.1 months).
- The safety profile of LentiGlobin treatment in severe SCD remains consistent with bone marrow harvest and myeloablative conditioning
  - Ten Grade 3 bone marrow harvest-related AEs were reported in three patients, including one SAE (pain/prolonged hospitalization)
  - Six patients experienced at least one SAE post-DP infusion
  - No AEs reported as related to LentiGlobin DP

### **Cerebral Adrenoleukodystrophy Program Updates**

bluebird bio also announced plans to expand enrollment by up to eight additional patients in the ongoing Starbeam Phase 2/3 clinical study of Lenti-D drug product in patients less than 18 years of age with cerebral adrenoleukodystrophy (CALD). The expansion of the study is intended to enable the first manufacture of Lenti-D in Europe and subsequent treatment of subjects in Europe, and to bolster the overall clinical data package for potential future regulatory filings in the United States and Europe. bluebird bio plans to begin treating additional patients in the Starbeam study in early 2017.

### **Webcast Information**

bluebird bio will host a live webcast at 8:30 p.m. PT (11:30 p.m. ET) today, December 5, 2016. The live webcast can be accessed under "Calendar of Events" in the Investors and Media section of the company's website at [www.bluebirdbio.com](http://www.bluebirdbio.com).

### **About TDT**

Transfusion-dependent  $\beta$ -thalassemia (TDT), also called  $\beta$ -thalassemia major or Cooley's anemia, is an inherited blood disease that can cause severe anemia and can be fatal within the first few years of life if not treated. TDT is one of the most common genetic diseases in the world, and approximately 60,000 children are born every year with a serious form of the disease.

Despite advances in the supportive conventional management of the disease, which consists of frequent and lifelong blood transfusions and iron chelation therapy, there is still a significant unmet medical need, including the risk for significant morbidity and

---



early mortality. Currently, the only advanced treatment option for transfusion-dependent  $\beta$ -thalassemia is allogeneic hematopoietic stem cell transplant (HSCT). Complications of allogeneic HSCT include a significant risk of treatment-related mortality, graft failure, graft vs. host disease (GvHD) and opportunistic infections, particularly in patients who undergo non-sibling-matched allogeneic HSCT.

#### **About SCD**

Sickle cell disease (SCD) is an inherited disease caused by a mutation in the beta-globin gene that results in sickle-shaped red blood cells. The disease is characterized by anemia, vaso-occlusive crisis, infections, stroke, overall poor quality of life and sometimes, early death.

Where adequate medical care is available, common treatments for patients with SCD largely revolve around management and prevention of acute sickling episodes. Chronic management may include hydroxyurea and, in certain cases, chronic transfusions. Given the limitations of these treatments, there is no effective long-term treatment. The only advanced treatment for SCD is allogeneic HSCT. Complications of allogeneic HSCT include a significant risk of treatment-related mortality, graft failure, GvHD and opportunistic infections, particularly in patients who undergo non-sibling-matched allogeneic HSCT.

#### **About the Starbeam (ALD-102) Study**

The Phase 2/3 Starbeam Study is assessing the efficacy and safety of Lenti-D, an investigational gene therapy, in boys up to 17 years of age with CALD. The study involves transplantation with a patient's own stem cells, which are modified to contain a functioning copy of the ABCD1 gene. This gene addition should result in the production of functional adrenoleukodystrophy protein (ALDP), a protein critical for the breakdown of very long chain fatty acids (VLCFAs). Buildup of VLCFAs in the central nervous system contributes to neurodegeneration in CALD.

Patients enrolled in the study are:

- Eligible for allogeneic hematopoietic stem cell transplant (HSCT) but with no matched sibling donor
- Have confirmed early-stage, active CALD as indicated by gadolinium enhancement on MRI
- Have a Loes score between 0.5 – 9.0
- Have an neurological function score (NFS) of one or less

The primary efficacy endpoint for the Starbeam study is the proportion of subjects who are alive and have none of six major functional disabilities (MFDs) at 24 months post treatment. MFDs are six symptoms captured in the Neurologic Function Score (NFS)

---



that, if present, are expected to severely affect the patient's capacity for independent living: loss of communication, cortical blindness, tube feeding, total incontinence, wheelchair dependence, and complete loss of voluntary movement.

### **About CALD**

Cerebral adrenoleukodystrophy (CALD) is a rare and commonly fatal, X-linked, genetic, neurodegenerative disease that primarily affects young boys. CALD involves a progressive destruction of myelin, the protective sheath of the nerve cells in the brain that are responsible for thinking and muscle control. Symptoms usually occur in early childhood and progress rapidly if untreated, leading to severe loss of neurological function and eventual death within 2-5 years in most patients. Early diagnosis is critical for boys to receive effective treatment. The worldwide incidence rate for ALD is approximately one in 21,000 male newborns; of those, 30-40% are affected by the cerebral form of the disease.

Currently, the only effective treatment option for patients with CALD is allogeneic HSCT. Complications of allogeneic HSCT include a significant risk of treatment-related mortality, graft failure, GvHD and opportunistic infections, particularly in patients who undergo non-sibling-matched allogeneic HSCT.

### **About bluebird bio, Inc.**

With its lentiviral-based gene therapies, T cell immunotherapy expertise and gene editing capabilities, bluebird bio has built an integrated product platform with broad potential application to severe genetic diseases and cancer. bluebird bio's gene therapy clinical programs include its Lenti-D™ product candidate, currently in a Phase 2/3 study, called the Starbeam Study, for the treatment of cerebral adrenoleukodystrophy, and its LentiGlobin™ BB305 product candidate, currently in four clinical studies for the treatment of transfusion-dependent  $\beta$ -thalassemia and severe sickle cell disease. bluebird bio's oncology pipeline is built upon the company's leadership in lentiviral gene delivery and T cell engineering, with a focus on developing novel T cell-based immunotherapies, including chimeric antigen receptor (CAR T) and T cell receptor (TCR) therapies. bluebird bio's lead oncology program, bb2121, is an anti-BCMA CAR T program partnered with Celgene. bb2121 is currently being studied in a Phase 1 trial for the treatment of relapsed/refractory multiple myeloma. bluebird bio also has discovery research programs utilizing megaTALs/homing endonuclease gene editing technologies with the potential for use across the company's pipeline.

---



bluebird bio has operations in Cambridge, Massachusetts; Seattle, Washington; 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 research, development, manufacturing and regulatory approval plans for its LentiGlobin product candidate to treat transfusion-dependent  $\beta$ -thalassemia and severe sickle cell disease and its Lenti-D product candidate to treat cerebral adrenoleukodystrophy, including statements whether the manufacturing process changes for LentiGlobin will improve outcomes of patients with transfusion-dependent  $\beta$ -thalassemia and severe sickle cell disease, whether the planned changes to the HGB-206 clinical trial protocol will improve outcomes in patients with severe sickle cell disease. 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, risks that the preliminary positive efficacy and safety results from our prior and ongoing clinical trials of LentiGlobin and Lenti-D will not continue or be repeated in our ongoing, planned or expanded clinical trials of LentiGlobin or the ongoing expanded clinical trial of Lenti-D, the risks that the changes we have made in the LentiGlobin manufacturing process or the HGB-206 clinical trial protocol will not result in improved patient outcomes, risks that the current or planned clinical trials of LentiGlobin and Lenti-D will be insufficient to support regulatory submissions or marketing approval in the US and EU, the risk of a delay in the enrollment of patients in our clinical studies, and the risk that any one or more of our product candidates will not be successfully developed, approved or commercialized. 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 quarterly report on 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.*

### **Contact:**

Investors:

bluebird bio, Inc.

Manisha Pai, 617-245-2107

mpai@bluebirdbio.com

Media:

bluebird bio, Inc.

Elizabeth Pingpank, 617-914-8736

---



[epingpank@bluebirdbio.com](mailto:epingpank@bluebirdbio.com)

or

Pure Communications, Inc.

Dan Budwick, 973-271-6085