

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): November 1, 2017

**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

(IRS Employer  
Identification No.)

60 Binney Street,  
Cambridge, MA  
(Address of Principal Executive Offices)

02142  
(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 (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))

Indicate by check mark whether the registrant is an emerging growth company as defined in 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 2.02 Results of Operations and Financial Condition**

On November 1, 2017, bluebird bio, Inc. announced its financial results for the three months ended September 30, 2017. A copy of the press release is being furnished as Exhibit 99.1 to this Current Report on Form 8-K, and is incorporated herein by reference.

The information in Item 2.02 of this Report on Form 8-K and Exhibit 99.1 attached hereto is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, except as expressly set forth by specific reference in such filing.

**Item 8.01 Other Events**

On November 1, 2017, bluebird bio, Inc. issued a press release announcing its abstract presentations at the 59<sup>th</sup> Annual meeting of the American Society of Hematology taking place on December 9-12, 2017. The full text of bluebird's press release regarding the announcement is filed at Exhibit 99.2 to Current Report on Form 8-K and is incorporated herein by reference.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	<a href="#">Press release issued by bluebird bio, Inc. on November 1, 2017</a>
99.2	<a href="#">Press release issued by bluebird bio, Inc. on November 1, 2017</a>

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**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: November 1, 2017

**bluebird bio, Inc.**

By: /s/ Jeffrey T. Walsh

Jeffrey T. Walsh

*Chief Financial & Strategy Officer and Principal Financial Officer*

**bluebird bio Reports Third Quarter 2017 Financial Results and Recent Operational Progress**

- 11 presentations across severe genetic diseases, immunotherapy and gene editing programs to be presented at the American Society of Hematology (ASH) Annual Meeting –
- Early data from patients treated under the amended study protocol in HGB-206 Phase 1 study in patients with severe sickle cell disease (SCD) suggest improved LentiGlobin drug product engraftment -
- Safety data observed in clinical study supports implementation of plerixafor mobilization in HGB-206 study protocol –
- Regenerative Medicine Advanced Therapy Designation granted by U.S. FDA for LentiGlobin drug product in SCD –
- Orphan drug designation granted for anti-BCMA CAR T therapy bb21217 –
- Ended quarter with \$1.1 billion in cash, cash equivalents and marketable securities –
- Company to hold conference call to discuss ASH abstracts and quarterly updates today, November 1, 8:30 am ET –

**CAMBRIDGE, Mass., November 1, 2017** – 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, today reported business highlights and financial results for the third quarter ended September 30, 2017.

“2017 has been a year focused on execution. In January, we outlined a set of goals intended to bring us closer to our 2022 vision of becoming the gene therapy products company,” said Nick Leschly, chief bluebird. “I’m pleased to say that we have accomplished many of these goals. We presented compelling data at ASCO, EHA and in the *New England Journal of Medicine* across all of our clinical programs, treated our first patient in the expansion cohort of our bb2121 Phase 1 multiple myeloma study and moved our second generation anti-BCMA CAR T program, bb21217, into the clinic. Coming into ASH, we have an early, but promising, indication that the changes we made in the HGB-206 study have had an improvement on engraftment and that mobilization and collection of stem cells using plerixafor may be a safe and viable option for patients with severe sickle cell disease. At ASH, we look forward to sharing additional data across our clinical programs as well as preclinical data that supports our future pipeline.”

**Recent Highlights**

- **ASH PRESENTATIONS** – Today, bluebird bio announced that the company will present clinical and pre-clinical data in 11 abstracts spanning the company’s research and development portfolio. Included among the presentations will be
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updated clinical data for the company's clinical studies of LentiGlobin: Northstar (HGB-204) in patients with transfusion-dependent  $\beta$ -thalassemia (TDT), HGB-205 in patients with TDT or severe sickle cell disease (SCD), Northstar-2 (HGB-207) in patients with TDT and non- $\beta^0/\beta^0$  genotypes and HGB-206 in patients with SCD. Updated data from the CRB-401 study of bb2121 anti-BCMA CAR T in patients with relapsed/refractory multiple myeloma will also be presented. The company will also present several preclinical and research posters.

- **HGB-206 UPDATED CLINICAL DATA** – In the abstracts announced today, early results from 2 patients treated in the HGB-206 study using a modified protocol with LentiGlobin drug product (DP) manufactured under a refined manufacturing process demonstrate both higher DP vector copy number (VCN) and higher peripheral VCN after transplant. The toxicity profile observed was consistent with myeloablative conditioning with single-agent busulfan.
  - **HGB-206 PLERIXAFOR SAFETY DATA** - Safety data exploring the use of plerixafor mobilization in 3 patients showed an acceptable safety profile and a larger cell dose yield. HGB-206 continues to enroll, and patients will be treated under the amended study protocol with DP made from cells obtained through apheresis following plerixafor mobilization.
  - **NORTHSTAR (HGB-204) UPDATED CLINICAL DATA** – ASH abstracts include updated results from the Phase 1/2 Northstar (HGB-204) study in patients with TDT using the original manufacturing process. The updated efficacy outcomes suggested that treatment with LentiGlobin drug product can potentially have a durable effect on eliminating or substantially reducing blood transfusions, and indicated that less favorable outcomes were seen in patients who had a low vector copy number (VCN). The safety profile continues to be consistent with autologous transplantation. No drug-product related adverse events (AEs) have been observed, and there is no evidence of clonal dominance.
  - **RMAT FOR LENTIGLOBIN IN SCD** – In October, the U.S. Food and Drug Administration (FDA) granted Regenerative Medicine Advanced Therapy Designation for LentiGlobin for the treatment of patients with severe SCD. Under this designation, the FDA will work closely with bluebird bio to provide guidance on the future development of LentiGlobin, including providing advice on generating the evidence needed to support potential approval of the product candidate.
  - **INTERIM LENTI-D DATA IN NEJM** – In October, bluebird bio announced the publication in the *New England Journal of Medicine* of interim clinical data on the initial 17 patients treated in the Starbeam study of Lenti-D drug product in cerebral adrenoleukodystrophy (CALD). These data were also presented at the Child Neurology Society (CNS) Annual Meeting. As of August 25, 2017, 15/17 patients (88%) in the initial study cohort remained free of major functional
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disabilities (MFDs) at 24 months, the primary endpoint of the trial. The safety profile of Lenti-D was consistent with myeloablative conditioning. No patients treated with Lenti-D had graft versus host disease (GvHD), and there was no graft rejection or clonal dominance. An expansion cohort of the Starbeam study is enrolling additional patients to enable the 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.

- **FIRST PATIENT TREATED IN BB21217 STUDY** - In September, bluebird bio announced that the first patient was treated in CRB-402, the company's Phase 1 study of bb21217 in patients with relapsed/refractory multiple myeloma. bb21217 is an anti-BCMA CAR T product candidate manufactured in the presence of a PI3 kinase inhibitor, designed to enrich for a more potent, longer-living T cell subtype that in preclinical *in vivo* studies showed improved anti-tumor activity. Subsequent to study initiation, in September Celgene exercised its option to exclusively license bb21217 resulting in a \$15 million option exercise payment from Celgene. Also in September, the U.S. Food and Drug Administration (FDA) granted orphan drug designation for bb21217.
- **CRB-401 ADVANCES TO EXPANSION COHORT** – In September, bluebird bio announced that the first patient was treated in the expansion cohort of CRB-401, the company's Phase 1 study of bb2121 anti-BCMA CAR T therapy in patients with relapsed/refractory multiple myeloma. Patients in the expansion cohort will be treated at a dose range of 150 to 450 x 10<sup>6</sup> CAR+ T cells and will be required to have prior exposure to a proteasome inhibitor, an immunomodulatory agent and daratumumab.
- **NEW BOARD APPOINTMENT** – In September, Mary Lynne Hedley, PhD, was appointed to the Board of Directors. bluebird bio also announced that with Dr. Hedley's appointment, John Maraganore, Ph.D. transitioned off the Board of Directors.

### Third Quarter 2017 Financial Results

- **Cash Position:** Cash, cash equivalents and marketable securities as of September 30, 2017 were \$1.1 billion, compared to \$884.8 million as of December 31, 2016, an increase of \$257.8 million.
  - **Revenues:** Total revenue was \$7.7 million for the third quarter of 2017 compared to \$1.6 million for third quarter of 2016. The increase is attributable to the commencement of revenue recognition for the bb2121 license and manufacturing services under the company's agreement with Celgene and revenue recognized under bluebird bio's out-licensing agreement with Novartis Pharma AG (Novartis). In August, Novartis received FDA approval of KYMRIAH™ and as a
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result, the company expects to recognize royalty revenue beginning in the fourth quarter of 2017.

- **R&D Expenses:** Research and development expenses were \$61.5 million for the third quarter of 2017 compared to \$64.0 million for the third quarter of 2016. The decrease in research and development expenses was attributable to decreased platform related expenses as a result of a one-time \$15.0 million upfront license payment expensed in the third quarter of 2016, partially offset by increased employee-related costs due to increased headcount to support overall growth, increased clinical trial costs, and increased facility related costs.
- **G&A Expenses:** General and administrative expenses were \$23.0 million for the third quarter of 2017 compared to \$14.6 million for the third quarter of 2016. The increase in general and administrative expenses was attributable to increased employee-related costs due to increased headcount to support overall growth, increased commercial-related costs attributable to market research costs, increased facility-related expenses, and increased professional and consulting fees.
- **Cost of License Revenue:** Cost of license revenue was \$1.1 million for the third quarter of 2017. Cost of license revenue is composed of amounts payable to third party licensors in connection with amounts received under our out-license arrangement with Novartis.
- **Net Loss:** Net loss was \$78.8 million for the third quarter of 2017 compared to \$77.0 million for the third quarter of 2016.

#### **Webcast Information**

bluebird bio will host a live webcast at 8:30 a.m. ET on Wednesday, November 1, 2017. 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). Alternatively, investors may listen to the call by dialing (844) 825-4408 from locations in the United States or (315) 625-3227 from outside the United States. Please refer to conference ID number 3795968.

#### **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 three clinical studies for the treatment of transfusion-dependent  $\beta$ -thalassemia, also known as  $\beta$ -thalassemia major, 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 programs,

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bb2121 and bb21217, are anti-BCMA CAR T programs partnered with Celgene. bb2121 and bb21217 are each currently being studied in Phase 1 trials 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 Europe.

LentiGlobin and Lenti-D are trademarks of bluebird bio, Inc. All other trademarks are the property of their respective owners.

#### **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 financial condition and results of operations, as well as the advancement of, and anticipated development and regulatory milestones and plans related to the Company's product candidates and clinical studies. 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 results from our clinical trials will not continue or be repeated in our ongoing clinical studies, the risk of cessation or delay of any of the ongoing or planned clinical studies and/or our development of our product candidates, the risk of a delay in the enrollment of patients in our clinical studies, the risks that the changes we have made in the LentiGlobin drug product manufacturing process or the HGB-206 clinical study protocol will not result in improved patient outcomes, risks that the current or planned clinical studies of the LentiGlobin drug product will be insufficient to support regulatory submissions or marketing approval in the United States and European Union, risks that the current clinical study of Lenti-D will be insufficient to support regulatory submissions or marketing approval in the United States and European Union, the risk that our collaborations, including our collaboration with Celgene, will not continue or will not be successful, 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 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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**bluebird bio, Inc.**  
**Condensed Consolidated Statements of Operations Data**  
**(unaudited)**  
**(in thousands, except per share data)**

	2017	Three Months Ended September 30,
<b>Revenues:</b>		
License revenue	\$ 2,500	
Collaboration revenue	5,211	
Total revenues	7,711	
<b>Operating expenses:</b>		
Research and development	61,545	
General and administrative	22,982	
Cost of license revenue	1,100	
Change in fair value of contingent consideration	(258)	
Total operating expenses	85,369	
Loss from operations	(77,658)	
Interest (expense) income, net	(1,155)	
Other (expense) income, net	8	
Loss before income taxes	(78,805)	
Income tax benefit	—	
Net loss	\$ (78,805)	
Net loss per share - basic and diluted:	\$ (1.73)	
Weighted-average number of common shares used in computing net loss per share - basic and diluted:		45,648



**bluebird bio, Inc.**  
**Condensed Consolidated Balance Sheets Data**  
**(unaudited)**  
**(in thousands)**

	As of September 30, 2017	As of December 31, 2016
Cash, cash equivalents and marketable securities	\$ 1,142,630	\$ 884,830
Total assets	1,405,756	1,118,122
Total liabilities	264,438	248,682
Total stockholders' equity	1,141,318	869,440

**Contact:**

Investors and Media:

bluebird bio, Inc.

Elizabeth Pingpank, 617-914-8736

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

**bluebird bio to Present New Data from Clinical Studies of LentiGlobin™ Gene Therapy in Transfusion-Dependent  $\beta$ -Thalassemia (TDT) and Severe Sickle Cell Disease (SCD) and bb2121 in Relapsed/Refractory Multiple Myeloma at American Society of Hematology (ASH) Annual Meeting**

- *11 total abstracts accepted, including updated data from Northstar-2 (HGB-207) Phase 3 study of LentiGlobin in patients with TDT and non- $\beta^0/\beta^0$  genotypes, HGB-205 study of LentiGlobin in patients with SCD and TDT, and CRB-401 study of bb2121 anti-BCMA CAR T in patients with relapsed/refractory multiple myeloma along with preclinical abstract data –*
- *Results from two subjects with SCD in LentiGlobin study HGB-206 treated under amended study protocol provide early indication of improved drug product vector copy numbers (DP VCN), in vivo VCN and HbA<sup>T87Q</sup> hemoglobin production –*
- *Clinical data indicate that use of single-agent plerixafor for stem cell mobilization is well tolerated by patients with SCD and may enable increased cell doses and a more favorable phenotype with fewer lineage committed lymphoid progenitors compared to bone marrow harvest; plerixafor mobilization clinical study cohort has been implemented in HGB-206 study -*
- *Data on patients with up to three-year follow up data from patients in the Northstar (HGB-204) study of LentiGlobin drug product in TDT demonstrate durability of treatment and potential for improved hemoglobin production over time –*
- *Company to hold conference call and webcast today, November 1, at 8:30 a.m. ET –*

**Cambridge, MA, November 1, 2017** – bluebird bio, Inc. (Nasdaq: BLUE), a clinical-stage company committed to developing potentially transformative gene therapies for serious genetic diseases and T cell-based immunotherapies for cancer, today announced that four oral and seven poster presentations will feature data from bluebird programs during the 59<sup>th</sup> Annual Meeting of the American Society for Hematology (ASH). The data will highlight bluebird’s advancement of its LentiGlobin product candidate in patients with transfusion-dependent  $\beta$ -thalassemia (TDT) and severe sickle cell disease (SCD), and its bb2121 product candidate in patients with relapsed/refractory multiple myeloma. Preliminary data from these abstracts will be available on the ASH conference [website](#) at 9:00 am ET today.

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“This year at ASH, we have the opportunity to share updated data across our clinical studies in severe genetic diseases and cancer, and to provide a look at some of the preclinical work that will inform the next phase of clinical development at bluebird,” said Dave Davidson, chief medical officer. “The new data in sickle cell disease suggest that the changes made to the HGB-206 protocol and to our manufacturing process are having a favorable impact on the engraftment of the gene-modified stem cells. The two patients treated in Group B have consistently higher DP VCN and *in vivo* VCN than Group A patients, and patient 1313 has the highest Month 3 HbA<sup>T87Q</sup> level seen to date in the study. We plan to share updated clinical data on these patients at ASH. Additionally, we are very encouraged by the emerging profile of plerixafor mobilization in patients with sickle cell disease. Early data show a more favorable safety profile and substantial improvement in the collection of CD34<sup>+</sup> cells compared to bone marrow harvest, suggesting that plerixafor may offer a more effective and less burdensome means to collect stem cells in patients with sickle cell disease.”

#### **Clinical Presentations Summary**

##### **Interim Results from a Phase 1/2 Clinical Study of LentiGlobin Gene Therapy for Severe Sickle Cell Disease (Oral Abstract #527)**

**Presenter:** Julie Kanter, M.D., Medical University of South Carolina, Charleston, SC

**Date & Time:** Sunday, December 10 at 5:30 pm

**Location:** Bldg C, Lvl 1, C101 Auditorium

##### **Abstract Results as of July 21, 2017:**

- 9 patients with severe SCD have received LentiGlobin drug product (DP). All successfully underwent bone marrow harvest (median 2 harvests, range 1–3) to collect the stem cells used to produce LentiGlobin drug product.
  - Patients in this study are divided into three cohorts: A, B and C. Patients in Group A were treated under the original study protocol. Patients in Group B were treated under an amended study protocol that included changes intended to address drug product vector copy number (VCN) and engraftment challenges seen in Group A. Patients in both Group A and B had drug product made from stem cells collected using bone marrow harvest. Group C will be composed of patients treated under the amended study protocol and with drug product made from stem cells collected using apheresis with plerixafor rather than via bone marrow harvest.
  - 7 patients were treated in Group A; initial results in these patients were presented at ASH 2016. The median cell dose was 2.1 (1.8–5.1) x 10<sup>6</sup> CD34<sup>+</sup> cells/kg, median DP VCN was 0.6 (0.3–1.3) copies/diploid genome, and 8%–42% CD34<sup>+</sup> cells were transduced. As of the data cutoff:
    - o Median follow-up was 18.3 (14.9–23.8) months since LentiGlobin infusion
    - o Median VCN in peripheral blood was 0.1 (0.1–0.2) copies/genome and median HbA<sup>T87Q</sup> level was 0.9 (0.4–2.4) g/dL at last measurement.
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- Patients experiencing multiple vaso-occlusive crises (VOCs) prior to study entry (n=6; median annualized frequency 4, range 2–28 VOCs annually) have had numerically fewer VOCs since LentiGlobin DP infusion (median annualized frequency 1, range 0–24 annually, 14%–100% reduction).
- 2 patients were treated in Group B. As of the data cutoff:
  - Patient 1313, whose DP VCNs were reported at ASH 2016, was treated with two DP lots, one of which was manufactured using the original process, and the other using the refined process.
    - The total DP cell dose was  $2.2 \times 10^6$  CD34+ cells/kg. DP VCNs were 1.4 (old process) and 3.3 (refined process) copies/genome. 46% (old process) and 83% (refined process) of CD34+ cells were transduced.
    - VCN in peripheral blood was 0.5 copies/genome and HbAT<sup>87Q</sup> level was 1.5 g/dL at 3 months after LentiGlobin infusion
  - Patient 1312 was treated with two DP lots manufactured using the refined process.
    - The total DP cell dose was  $3.2 \times 10^6$  CD34+ cells/kg. DP VCNs were 5.0 and 2.9 copies/genome. 95% and 90% of CD34+ cells were transduced.
    - VCN in peripheral blood was 2.6 copies/genome at 1 month after LentiGlobin infusion.
    - HbAT<sup>87Q</sup> was not yet available at time of data cut for abstract
- Additional patients (Group C) have been enrolled in HGB-206 as of July 21, 2017. Additional data including mobilization results and DP characteristics for these patients will also be presented at ASH.
- The toxicity profile observed from start of conditioning to latest follow-up was consistent with myeloablative conditioning with single-agent busulfan.

**Successful Plerixafor-Mediated Mobilization, Apheresis, and Lentiviral Vector Transduction of Hematopoietic Stem Cells in Patients with Severe Sickle Cell Disease (Poster Abstract #990)**

**Presenter:** John Tisdale, M.D., National Heart, Lung and Blood Institute (NHLBI), Bethesda, MD

**Date & Time:** Saturday, December 9 at 5:30 pm

**Location:** Bldg A, Lvl 1, Hall A2

**Abstract Results:**

- Three patients with severe sickle cell disease (SCD) have undergone plerixafor mobilization.
  - A total of  $15.3$ ,  $5.6$ , and  $9.0 \times 10^6$  CD34+ cells/kg were collected in a single day of apheresis. In contrast, bone marrow harvest collections for all prior patients in the study yielded a mean of  $5.0$  (range  $0.3$ – $10.8$ )  $\times 10^6$  CD34+ cells/kg per harvest (N=21).
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- *Ex vivo* cultured CD34<sup>+</sup> cells isolated from bone marrow harvests consisted of an average of 41.0% (17.3%—50.7%) CD34<sup>dim</sup> cells. In contrast, *ex vivo* cultured CD34<sup>+</sup> cells isolated from plerixafor mobilized peripheral blood (PB) contained an average of 8.2% (1.5—19.5%) CD34<sup>dim</sup> cells. CD34<sup>dim</sup> cells, which express low levels of CD34, are generally less primitive/less likely to be true primitive stem cells than other CD34<sup>+</sup> positive cells.
- Similar drug product vector copy numbers were observed after research-scale transduction of CD34<sup>+</sup> cells collected from a bone marrow harvest and from plerixafor mobilized cells from the same patient.

The mobilization and apheresis procedures had an acceptable toxicity profile. No dose-limiting toxicities were observed after plerixafor dosing.

### **Clinical Outcomes up to 3 Years Following LentiGlobin Gene Therapy for Transfusion-Dependent $\beta$ -Thalassemia in the Northstar HGB-204 Study (Oral Abstract #360)**

**Presenter:** Janet Kwiatowski, M.D., MSCE, Children's Hospital of Philadelphia, Philadelphia, PA

**Date & Time:** Sunday, December 10 at 10:45 am

**Location:** Building B, Lvl 2, B213-B214

#### **Abstract Results, as of June 2, 2017:**

- As previously reported, the study has completed its treatment phase and eighteen patients with TDT (8 with  $\beta^0/\beta^0$  and 10 with non- $\beta^0/\beta^0$  genotypes) received LentiGlobin drug product (DP).
  - The median drug product vector copy number (VCN) was 0.7 (range: 0.3–1.5) copies/diploid genome, the median cell dose was 8.1 (range: 5.2–18.1)  $\times 10^6$  CD34<sup>+</sup> cells/kg, and the proportion of transduced CD34<sup>+</sup> cells was 17–58%.
  - Of the 10 patients with non- $\beta^0/\beta^0$  genotypes, 8 have been free of transfusions for a median of 27.1 (range 12.5–35.2) months.
  - The 2 patients with non- $\beta^0/\beta^0$  genotypes who still require intermittent transfusions had annual transfusion volumes reduced by 30% and 94%; both received DP with a VCN in the lower range (DP VCNs: 0.3 and 0.4 copies/diploid genome).
  - Two patients with  $\beta^0/\beta^0$  genotypes have not received a transfusion in more than a year. At the patients' last study visit (Month 24/Month 12), total Hb levels were 9.0 and 10.2 g/dL, HbA<sup>T87Q</sup> levels were 8.2 and 6.8 g/dL, and peripheral VCNs were 0.9 and 0.6, respectively.
  - Six patients with  $\beta^0/\beta^0$  genotypes have continued transfusions. Their annual transfusion volumes have decreased by a median of 63% (range: 19% to 81%).
  - The safety profile continues to be consistent with myeloablative conditioning with single-agent busulfan. No drug-product related serious adverse events (AEs) have been observed, and there is no evidence of clonal dominance.
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### **Additional Clinical Presentations**

**Results from the HGB-207 (Northstar-2) Trial: A Phase 3 Study to Evaluate Safety and Efficacy of LentiGlobin Gene Therapy for Transfusion-Dependent  $\beta$ -thalassemia (TDT) in Patients with non- $\beta^0/\beta^0$  Genotypes (Oral Abstract #526)**

**Presenter:** Mark C. Walters, M.D., UCSF Benioff Children's Hospital, Oakland, Calif

**Date & Time:** Sunday, December 10 at 5:15 pm

**Location:** Bldg C, Lvl 1, C101 Auditorium

*Abstract contains data presented at European Hematology Association (EHA) 2017 annual meeting. Updated data to be included in ASH presentation.*

**Longer Term Follow-up on the First Patients with Severe Hemoglobinopathies Treated with LentiGlobin Gene Therapy (Poster Abstract #4609)**

**Presenter:** Marina Cavazzana, M.D., Necker-Enfants Malades Hospital, Paris, France

**Date & Time:** Monday, December 11 at 6:00 pm

**Location:** Bldg A, Lvl 1, Hall A2

*Abstract contains data presented at European Hematology Association (EHA) 2017 annual meeting. Updated data to be included in ASH presentation.*

**Durable clinical responses in heavily pretreated patients with relapsed/refractory multiple myeloma: Updated results from a multicenter study of bb2121 anti-BCMA CAR T cell therapy (Oral Abstract #740)**

**Presenter:** Jesus Berdeja, M.D., Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN

**Date & Time:** Monday, December 11 at 3:00 pm

**Location:** Bldg C, Lvl 1, Hall C1

*Abstract contains data presented at American Society of Clinical Oncology (ASCO) 2017 annual meeting. Updated data to be included in ASH presentation.*

### **Preclinical Presentations**

**Preclinical Evaluation of a Novel Lentiviral Vector Driving Lineage-Specific BCL11A Knockdown  $\gamma$ -Globin Induced and Simultaneous Repression of  $\beta$ -Globin for the Potential Treatment of Sickle Cell Disease (Poster Abstract #3557)**

**Presenter:** Olivier Negre, Ph.D., bluebird bio

**Date & Time:** Monday, December 11 at 6:00 pm

**Location:** Bldg A, Lvl 1, Hall A2

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**A novel TGF- $\beta$ /interleukin receptor signal conversion platform that protects CAR/TCR T cells from TGF- $\beta$ -mediated immune suppression and induces T cell supportive signaling networks (Poster Abstract #1911)**

**Presenter:** Benjamin Boyerinas, Ph.D., bluebird bio

**Date & Time:** Saturday, December 9 at 5:30 pm

**Location:** Bldg A, Lvl 1, Hall A2

**A Drug-Regulated CAR Platform (DARIC) Induces Effective and Reversible Tumor Control In Vivo Using Non-Immunosuppressive Rapamycin Dosing (Poster Abstract #1910)**

**Presenter:** Unja Martin, Ph.D., bluebird bio

**Date & Time:** Saturday, December 9 at 5:30 pm

**Location:** Bldg A, Lvl 1, Hall A2

**Gene Editing of TRAC Locus Utilizing megaTAL Nucleases Increases Expression of Transgenic TCRs Delivered via Lentiviral Vector-Mediated Gene Transfer (Poster Abstract #1906)**

**Presenter:** Michael Magee, Ph.D., bluebird bio

**Date & Time:** Saturday, December 9 at 5:30 pm

**Location:** Bldg A, Lvl 1, Hall A2

**ROR1-directed chimeric antigen receptor T cell recognition of self-antigen is associated with acute toxicity, T cell dysfunction, and poor tumor control (Poster Abstract #4450)**

**Presenter:** James Rottman, Ph.D., bluebird bio

**Date & Time:** Monday, December 11 at 6:00 pm

**Location:** Bldg A, Lvl 1, Hall A2

**Webcast Information**

bluebird bio will host a live webcast at 8:30 a.m. ET on Wednesday, November 1, 2017. 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). Alternatively, investors may listen to the call by dialing (844) 825-4408 from locations in the United States or (315) 625-3227 from outside the United States. Please refer to conference ID number 3795968.

**About TDT**

Transfusion-dependent  $\beta$ -thalassemia (TDT), also called Cooley's anemia, is a rare and severe genetic blood disease.

Despite the availability of lifelong supportive care with blood transfusions and chelation treatments, many people with TDT experience serious complications and organ damage due to underlying disease and iron overload.

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Allogeneic hematopoietic stem cell transplant (HSCT) is currently the only available option to address the underlying cause of TDT, though it carries significant risks. 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. Common complications include 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 prevention of infection and management and prevention of acute sickling episodes. Chronic management may include hydroxyurea pharmacotherapy 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 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 three clinical studies for the treatment of transfusion-dependent  $\beta$ -thalassemia, also known as  $\beta$ -thalassemia major, 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 programs, bb2121 and bb21217, are anti-BCMA CAR T programs partnered with Celgene. bb2121 and bb21217 are each currently being studied in Phase 1 trials 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 Europe.

LentiGlobin and Lenti-D are trademarks of bluebird bio, Inc.

**Forward-Looking Statements**

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*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 bb2121 product candidate to treat relapsed/refractory multiple myeloma, 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, including plerixafor mobilization, 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, the risks that the preliminary positive efficacy and safety results from our prior and ongoing clinical trials of LentiGlobin will not continue or be repeated in our ongoing, planned or expanded 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, including our bb2121 product candidate, 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 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:**  
bluebird bio  
Investors & Media  
Elizabeth Pingpank, 617-914-8736  
[epingpank@bluebirdbio.com](mailto:epingpank@bluebirdbio.com)