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**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 13, 2015**

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**bluebird bio, Inc.**

(Exact name of registrant as specified in its charter)

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**DELAWARE**

(State or other jurisdiction of  
incorporation)

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**001-35966**

(Commission File Number)

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**13-3680878**

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

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**150 Second Street  
Cambridge, MA**

(Address of principal executive offices)

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**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)

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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:

- 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))
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**Item 7.01 Regulation FD Disclosure.**

On June 15, 2015, bluebird bio, Inc. (“bluebird”) issued a press release announcing Dr. Philip Gregory’s appointment as bluebird’s Chief Scientific Officer. A copy of this press release is furnished as Exhibit 99.2 to this report on Form 8-K.

On June 15, 2015, bluebird conducted an investor webcast summarizing clinical data from its HGB-205 clinical trial that was presented at an oral presentation at the 20<sup>th</sup> European Hematology Association Congress in Vienna, Austria on June 13, 2015. A copy of the presentation is being furnished as Exhibit 99.3 to this Report on Form 8-K.

The information in Item 7.01 of this Report on Form 8-K and Exhibits 99.2 and 99.3 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 June 13, 2015, bluebird issued a press release announcing clinical data from its HGB-205 clinical trial at an oral presentation at the 20<sup>th</sup> European Hematology Association Congress in Vienna, Austria on June 13, 2015. The full text of bluebird’s 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.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press release issued by bluebird bio, Inc. on June 13, 2015.
99.2	Press release issued by bluebird bio, Inc. on June 15, 2015.
99.3	Investor presentation provided by bluebird bio, Inc. on June 15, 2015.

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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: June 15, 2015

**bluebird bio, Inc.**

By: /s/ Jason F. Cole  
Jason F. Cole  
*Senior Vice President, General Counsel*

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## EXHIBIT INDEX

<u>Exhibit No.</u>	<u>Description</u>
99.1	Press release issued by bluebird bio, Inc. on June 13, 2015.
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99.3	Investor presentation provided by bluebird bio, Inc. on June 15, 2015.



## **Exhibit 99.1**

### **bluebird bio Reports New Beta-thalassemia Major and Severe Sickle Cell Disease Data from HGB-205 Study at EHA**

- *Patient with Severe Sickle Cell Disease Producing 45% Anti-sickling Hemoglobin at Six Months and Has Been Free of Transfusions for More Than Three Months*
- *Patients with Beta-thalassemia Major Remain Transfusion-Independent at 16 and 14 Months, Respectively*
- *First Patient with Severe Sickle Cell Disease Infused in HGB-206 Study*
- *Investor Conference Call Scheduled for June 15, 2015 at 8:00 a.m. ET*

**VIENNA, Austria and CAMBRIDGE, Mass.**, June 13, 2015 – bluebird bio, Inc. (Nasdaq: BLUE), a clinical-stage company committed to developing potentially transformative gene therapies for severe genetic and rare diseases and T cell-based immunotherapies, today announced long-term follow up of two patients with beta-thalassemia major and early safety and efficacy data in the first patient with severe sickle cell disease (SCD) treated with LentiGlobin BB305 product candidate in the HGB-205 study. These data were presented today at the 20th Congress of the European Hematology Association (EHA) in Vienna, Austria by Marina Cavazzana, M.D., Ph.D., lead investigator of the HGB-205 study and professor of hematology at Paris Descartes University, head of the department of Biotherapy Hospital, the clinical research INSERM center of Biotherapy at Necker Enfants Malades, (Assistance Publique-Hôpitaux de Paris) and the Lymphohematopoiesis Laboratory, Institute of Genetic Diseases, Imagine, Paris, France.

#### **Key findings:**

- **Beta-thalassemia:**
  - As of May 2015, Subjects 1201 and 1202 with beta-thalassemia major remained transfusion-independent for 16 and 14 months, respectively, with persistent stable expression of HbA<sup>T87Q</sup>. Neither has experienced a LentiGlobin-related adverse event.
- **Sickle Cell Disease:**
  - The proportion of anti-sickling hemoglobin being produced by the first-ever patient with severe SCD treated with gene therapy (Subject 1204) is rising steadily and accounted for 45% of all hemoglobin production (40% HbA<sup>T87Q</sup> + 5% HbF) at the patient's six-month visit post-drug product infusion; this is above the 30% threshold expected to potentially achieve a disease-modifying clinical effect.
  - As of May 2015, Subject 1204 had been free of transfusions for more than three months without complications or hospitalizations for SCD-related events post-transplant, and with improvement in hemolysis markers



“These data are promising for patients living with beta-thalassemia major and severe sickle cell disease, two devastating, genetically-based hematologic diseases that have a profound impact on both quality of life and life expectancy,” said Professor Cavazzana. “The steady rise and high-level of HbA<sup>T87Q</sup> production in our patient with severe sickle cell disease is cause for optimism as we expect levels of anti-sickling hemoglobin of 30 percent or more could significantly improve and potentially eliminate the serious and life-threatening complications associated with sickle cell disease.”

bluebird bio also announced that the first patient with severe SCD has been infused in the HGB-206 U.S.-based clinical study at the National Institutes of Health Clinical Center in Bethesda, Maryland. HGB-206 is a Phase 1, U.S.-based clinical trial evaluating the safety and efficacy of bluebird bio’s LentiGlobin BB305 product candidate in subjects with severe SCD.

“Today’s data further demonstrate the potentially transformative effects of gene therapy for the treatment of beta-hemoglobinopathies and support our global regulatory strategy for LentiGlobin in beta-thalassemia major, with the goal of potentially accelerated approvals in the EU and U.S.,” said David Davidson, M.D., chief medical officer, bluebird bio. “We are excited that the promising early results for LentiGlobin in beta-thalassemia major are now extending to the first treated patient with severe sickle cell disease. With the treatment of the first patient with severe sickle cell disease in the HGB-206 study, we look forward to gaining increasing clarity on the potential clinical benefit of LentiGlobin for patients with severe sickle cell disease.”

#### **HGB-205 Study Data**

HGB-205 is an ongoing, open-label, single-center Phase 1/2 study designed to evaluate the safety and efficacy of LentiGlobin BB305 product candidate for the treatment of patients with beta-thalassemia major and severe SCD. As of May 2015, two patients with beta-thalassemia major and one patient with severe SCD have undergone infusion with LentiGlobin BB305 product candidate in this study.

- *Patients with beta-thalassemia major demonstrated continued transfusion independence:* The data presented today are an update on those initially presented at EHA in June 2014 and demonstrate a long-term stable and durable response. As reported at ASH in December 2014, Subjects 1201 and 1202 achieved rapid transfusion independence with near-normal hemoglobin levels. As of May 2015, Subjects 1201 and 1202 remained transfusion independent for 16 and 14 months, respectively.
  - *Early efficacy data is promising in the first subject with severe SCD treated with gene therapy:* The production of anti-sickling hemoglobin is consistent with a level expected to potentially achieve a disease-modifying clinical effect in Subject
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1204. At the six-month visit post-drug product infusion, the proportion of anti-sickling hemoglobin (HbAT87Q + HbF) accounted for 45% of all hemoglobin production (40% HbAT87Q + 5% HbF). The patient's vector copy number in peripheral blood leukocytes was 2.2.

- Subject 1204 had his last red blood cell (RBC) transfusion at day 88. Since his infusion with LentiGlobin, this patient has had no hospitalizations, and has demonstrated improvements in markers of hemolysis, including normalization of reticulocyte count (from 283.3 x 10<sup>9</sup>/L to 131.7 x 10<sup>9</sup>/L) and lactate dehydrogenase (LDH) (from 626 U/L to 254 U/L).

	Beta Thalassemia Major		Severe Sickle Cell Disease
<b>Patient</b>	1201	1202	1204
<b>Enrollment age/Sex</b>	18/F	16/M	13/M
<b>Country of Origin</b>	Syria	France	France
<b>Genotype</b>	B0/BE	B0/BE	BS/BS
<b>Transfusion requirements (mls/kg/year)</b>	139	188	170
<b>CD34+ VCN in drug substance</b>	1.5	2.1	1.2/1.0*
<b>CD34+ cell count (x10<sup>6</sup>/kg) in drug substance</b>	8.9	13.6	5.6
<b>Days to neutrophil engraftment</b>	Day +13	Day +15	Day +37
<b>HbAT87Q/total Hb (g/dL) at last visit</b>	7.3/10.5	9.7/12.8	4.3/10.6
<b>Last study follow up (months)**</b>	15	15	6

*\*If more than one drug substance was manufactured for a subject, the VCN of each drug substance lot is quantified and the cell count is combined.*

*\*\* Last scheduled study visit for which results were available as of May 2015*

In the HGB-205 study, treatment with our LentiGlobin BB305 product candidate has been well-tolerated to-date, with no LentiGlobin-related adverse events observed. All of the adverse events observed are consistent with myeloablative conditioning.

All three subjects successfully engrafted and insertional site analyses (ISAs) demonstrate highly polyclonal reconstitution without clonal dominance.

#### **Investor Conference Call and Webcast Information**

bluebird bio will host a conference call and webcast on Monday, June 15 at 8:00 a.m. ET to review the data presented at EHA. The event will be webcast live and 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 and (315) 625-3227 from outside the United States.

### **About Beta-thalassemia**

Beta-thalassemia is an inherited blood disease that can cause severe anemia. Patients with beta-thalassemia cannot make enough of the beta-globin part of hemoglobin, the protein used by red blood cells to carry oxygen throughout the body. Approximately 60,000 children are born with a serious form of the disease every year, making it one of the most common genetic diseases in the world. In its most severe form, beta-thalassemia is fatal if not treated.

Treating beta-thalassemia includes frequent and lifelong blood transfusions, which deliver red blood cells to the body to correct the anemia. However, blood transfusions also cause excess iron to build up in the body, which can damage organs and cause additional issues, such as abdominal pain, weakness, fatigue, joint pain, endocrine dysfunction, liver cirrhosis and heart failure. Patients who receive ongoing blood transfusions must also receive treatment to remove the excess iron. The only currently available curative treatment option for beta-thalassemia is allogeneic hematopoietic stem cell transplant. However, these transplants are typically offered to pediatric patients with matched related donors (occurring in less than 25 percent of all cases), due to the significant risk of transplant-related morbidity and mortality.

### **About Sickle Cell Disease**

Sickle cell disease (SCD) is a hereditary blood disorder resulting from a mutation in the beta-globin gene that causes polymerization of hemoglobin proteins and abnormal red blood cell function. The symptoms of SCD include anemia, vaso-occlusive crises (a painful complication caused by obstruction of the blood vessels), infections, stroke, and progressive end-organ damage leading to overall poor quality of life and early death in a large subset of patients. The global incidence of SCD is estimated to be 300,000 births annually, and the global prevalence of the disease is estimated to be about 25 million.

Patients with severe SCD typically receive chronic blood transfusion regimens or hydroxyurea. Chronic transfusions for SCD introduce the risk of iron overload, which over time contributes to mortality through iron-associated heart and liver toxicity, and patients must adhere to daily iron chelation regimens. While hydroxyurea has been shown to significantly reduce the burden of vaso-occlusive crisis and related complications, it does not eliminate them. The only potentially curative therapy is allogeneic hematopoietic stem cell transplant (HSCT). Because of the significant morbidity and mortality risks associated with transplants, they are usually offered only to patients who have sibling matched donors and only 10 percent of SCD patients of African descent are able to find such donors.

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**About the HGB-205 Study**

HGB-205 is an ongoing, open-label Phase 1/2 study designed to evaluate the safety and efficacy of bluebird bio's LentiGlobin BB305 product candidate in the treatment of subjects with beta-thalassemia major and severe sickle cell disease (SCD). The study is designed to enroll up to seven subjects who will be followed to evaluate safety and transfusion requirements post-transplant. Among patients with SCD only, efficacy will also be measured based on the number of vaso-occlusive crises or acute chest syndrome events. For more information on the HGB-205 study, please visit [clinicaltrials.gov](https://clinicaltrials.gov) using identifier NCT02151526.

**About the HGB-206 Study**

HGB-206 is an ongoing, open-label Phase 1 study designed to evaluate the safety and efficacy of LentiGlobin BB305 product candidate in the treatment of subjects with severe sickle cell disease (SCD). The study is designed to enroll up to eight subjects to evaluate safety and efficacy as measured by changes in red cell function tests and hemolysis markers, as well as clinical events secondary to SCD, including vaso-occlusive crises or acute chest syndrome events. For information on the HGB-206 study, please visit [clinicaltrials.gov](https://clinicaltrials.gov) using the identifier NCT02140554.

**About bluebird bio, Inc.**

With its lentiviral-based gene therapy and gene editing capabilities, bluebird bio has built an integrated product platform with broad potential application to severe genetic diseases and T cell-based immunotherapy. bluebird bio's clinical programs include Lenti-D™, currently in a Phase 2/3 study, called the Starbeam Study, for the treatment of childhood cerebral adrenoleukodystrophy, and LentiGlobin®, currently in three clinical studies: a global Phase 1/2 study, called the Northstar Study, for the treatment of beta-thalassemia major; a single-center Phase 1/2 study in France (HGB-205) for the treatment of beta-thalassemia major or severe sickle cell disease; and a separate U.S. Phase 1 study for the treatment of sickle cell disease (HGB-206). bluebird bio also has ongoing preclinical CAR T immuno-oncology programs, as well as discovery research programs utilizing megaTALs/homing endonuclease gene editing technologies.

bluebird bio has operations in Cambridge, Massachusetts, Seattle, Washington, and Paris, France. For more information, please visit [www.bluebirdbio.com](http://www.bluebirdbio.com).

**About the Institute of Genetic Diseases -- *Imagine***

Imagine is a research and innovative healthcare institute of a new type, bringing together researchers, doctors and patients, with a common goal: to cure genetic diseases. This new Institute is housed in a 19,000 m<sup>2</sup> building located on the campus of the Necker Enfants Malades Hospital, and brings together over 850 researchers, doctors and healthcare personnel, with an innovative vision: gathering all those concerned in the treatment of genetic diseases to create synergy that encourages transfer of knowledge, to speed up the discovery of new treatments and diagnoses to meet the expectations of the patients and their families.

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## **About the AP-HP**

AP-HP, Greater Paris University Hospital, is a care provider known worldwide with its 38 hospitals and the largest university medical center in France and in Europe. Each year, AP-HP welcomes 7 million patients, takes care of more than 1.1 million emergencies and makes more than 5 million outpatient visits. AP-HP is the largest employer in Paris Region with 95,000 people -- doctors, researchers, paramedical, administrative staff and workers.

## ***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 potential efficacy and safety of the Company’s LentiGlobin product candidate, in subjects with beta thalassemia major and severe sickle cell disease, including statements concerning the reduced or eliminated need for transfusion support for the study subjects and the potential reduction in symptoms of severe sickle cell disease, statements concerning the Company’s future plans with respect to LentiGlobin and its other product candidates and statements concerning the HGB-206 clinical trial in severe sickle cell disease. It should be noted that the data for LentiGlobin announced from the HGB-205 study at the EHA Congress are preliminary in nature and the Northstar, HGB-205 and HGB-206 studies LentiGlobin are not completed. There is limited data concerning long-term safety and efficacy following treatment with LentiGlobin drug product. These data may not continue for these subjects or be repeated or observed in ongoing or future studies involving our LentiGlobin product candidate, including the HGB-205 Study, the Northstar Study or the HGB-206 study in severe sickle cell disease. It is possible that subjects for whom transfusion support has been reduced or eliminated may receive transfusion support in the future and that the subject with severe sickle cell disease may experience serious symptoms of the 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 risk that the preliminary results from our clinical trials will not continue or be repeated in our ongoing clinical trials, the risk that previously conducted studies involving similar product candidates will not be repeated or observed in ongoing or future studies involving current product candidates, 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 the Company’s clinical studies, the risk that 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 and 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

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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.

**Investor Relations:**

Manisha Pai  
bluebird bio, Inc.  
(617) 245-2107  
[mpai@bluebirdbio.com](mailto:mpai@bluebirdbio.com)

**Media:**

Dan Budwick  
Pure Communications, Inc.  
(973) 271-6085



**Philip Gregory, D. Phil., Joins bluebird bio as Chief Scientific Officer**

CAMBRIDGE, Mass., June 15, 2015 – bluebird bio, Inc. (Nasdaq: BLUE), a clinical-stage company committed to developing potentially transformative gene therapies for severe genetic and rare diseases and T cell-based immunotherapies, today announced that Philip Gregory, D. Phil., is joining the company as its Chief Scientific Officer and a member of the leadership team.

Dr. Gregory comes to bluebird bio from Sangamo BioSciences Inc., where he most recently served as Chief Scientific Officer and Senior Vice President, Research. At Sangamo, Dr. Gregory was responsible for setting the scientific direction of the company, prosecuting the development of the company’s genome editing platform and overseeing the early discovery and development of IND candidates.

“Philip brings a wealth of pioneering leadership and expertise in the field of genome editing and gene therapy to bluebird bio during an exciting point in our company’s growth,” said Nick Leschly, chief bluebird. “Philip shares our unwavering commitment to deliver therapies that have the potential to transform the lives of patients. The breadth and depth of his knowledge and experience will be crucial as we build a leading gene therapy products company.”

“bluebird bio is uniquely positioned with deep expertise and a broad platform across lentiviral vectors and genome editing, with numerous promising therapeutic applications,” said Dr. Gregory. “I am excited to be part of the team that is building and expanding upon this foundational work to bring potentially transformative therapies to patients.”

Dr. Gregory holds a D.Phil. in Biochemistry from Oxford University, and B.Sc. in Microbiology from Sheffield University.

**About bluebird bio, Inc.**

With its lentiviral-based gene therapy and gene editing capabilities, bluebird bio has built an integrated product platform with broad potential application to severe genetic diseases and T cell-based immunotherapy. bluebird bio’s clinical programs include Lenti-D™, currently in a Phase 2/3 study, called the Starbeam Study, for the treatment of childhood cerebral adrenoleukodystrophy, and LentiGlobin®, currently in three clinical studies: a global Phase 1/2 study, called the Northstar Study, for the treatment of beta-thalassemia major; a single-center Phase 1/2 study in France (HGB-205) for the treatment of beta-thalassemia major or severe sickle cell disease; and a separate U.S. Phase 1 study for the treatment of sickle cell disease (HGB-206). bluebird bio also has ongoing preclinical CAR T immuno-oncology programs, as well as discovery research programs utilizing megaTALs/homing endonuclease gene editing technologies.

bluebird bio has operations in Cambridge, Massachusetts, Seattle, Washington, and Paris, France. For more information, please visit [www.bluebirdbio.com](http://www.bluebirdbio.com).

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**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 research, development and advancement of bluebird bio's product candidates and research programs. 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 bluebird bio's research programs will be unsuccessful and not identify any viable product candidates or will not be safe or effective in clinical trials, the risk of cessation or delay of any of the planned clinical studies and/or our development of our product candidates, the risk of a delay in the enrollment of patients in the Company’s clinical studies, the risk that our collaboration with Celgene around anti-BCMA product candidates 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 and 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 annual 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.

**Availability of other information about bluebird bio**

Investors and others should note that we communicate with our investors and the public using our company website ([www.bluebirdbio.com](http://www.bluebirdbio.com)), our investor relations website (<http://www.bluebirdbio.com/investor-splash.html>), including but not limited to investor presentations and FAQs, Securities and Exchange Commission filings, press releases, public conference calls and webcasts. You can also connect with us on Twitter @bluebirdbio, LinkedIn or our YouTube channel. The information that we post on these channels and websites could be deemed to be material information. As a result, we encourage investors, the media, and others interested in bluebird bio to review the information that we post on these channels, including our investor relations website, on a regular basis. This list of channels may be updated from time to time on our investor relations website and may include other social media channels than the ones described above. The contents of our website or these channels, or any other website that may be accessed from our website or these channels, shall not be deemed incorporated by reference in any filing under the Securities Act of 1933.

**Investor Relations:**

Manisha Pai  
bluebird bio, Inc.  
(617) 245-2107  
[mpai@bluebirdbio.com](mailto:mpai@bluebirdbio.com)

**Media:**

Dan Budwick  
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(973) 271-6085



bluebirdbio®

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*Making Hope a Reality*

**Transforming the Lives of Patients**

with Severe Genetic and Rare Diseases

**EHA 2015 Clinical Data Update**

Nasdaq : BLUE

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# Forward Looking Statement

These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward looking statements. For example, all statements we make regarding the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, our ability to advance product candidates into, and successfully complete, clinical studies, and the timing or likelihood of regulatory filings and approvals are forward looking.

All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These statements are also subject to a number of material risks and uncertainties that are described in our most recent quarterly report on Form 10-Q, as well as our subsequent filings with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

Nasdaq: BLUE

# bluebird bio: Why We Do What We Do



Ethan



Aidan



Cameron

## *Our Vision – Make Hope a Reality*

*Seeking to transform the lives of patients with severe genetic and rare diseases through the development of innovative gene therapy products.*





# bluebird Pipeline Overview

Product Candidates	Program Area	Preclinical	Phase 1/2	Phase 2/3	Rights/Partner
<b>Lenti-D™</b>	CNS Diseases				
	Childhood Cerebral ALD				Worldwide
<b>LentiGlobin®</b>	Rare Hemoglobinopathies				
	β-thalassemia Major*				Worldwide
	Severe Sickle Cell Disease				Worldwide
<b>bb2121 BCMA</b>	Oncology				
	Multiple Myeloma				Celgene
	Next Gen BCMA				Celgene
	Five Prime Target				Worldwide
<b>Other Programs</b>					Worldwide
<b>Early Pipeline</b>	Research				
	Undisclosed + Gene Editing				Worldwide

\* The current clinical trials for LentiGlobin are Phase 1/2 studies that may provide the basis for early conditional approval in some jurisdictions

# Recent Events and Milestones

- ✓ Accelerated regulatory pathway for LentiGlobin in  $\beta$ -thalassemia defined for U.S. and EU
- ✓ Achieved enrollment targets in Starbeam Study (CCALD) and Northstar Study ( $\beta$ -thalassemia major)
- ✓ Defined oncology strategy – BCMA 1<sup>st</sup> CAR T Program; Five Prime target; bluebird independent pathway
- ✓ Presented first SCD data at EHA (Abstract 5/18; EHA presentation 6/13); infused 1<sup>st</sup> patient in HGB-206
- ✓ Appointed Philip Gregory, D.Phil., as Chief Scientific Officer

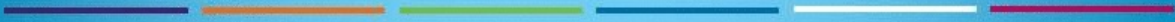
# New CSO Appointed

- 15 years of experience in biopharmaceutical industry
- Extensive gene therapy and genome editing experience
- Formerly Chief Scientific Officer and Senior Vice President of Research at Sangamo BioSciences
- D.Phil. in Biochemistry from Oxford University; B.Sc. in Microbiology from Sheffield University



**Philip Gregory, D. Phil.  
Chief Scientific Officer**

# EHA Data Update



## Data Demonstrate Continued Promise of Gene Therapy in Beta-thalassemia Major; First Patient with Severe Sickle Cell Disease Treated with Gene Therapy

### EHA 2015: Updated data from three patients in HGB-205

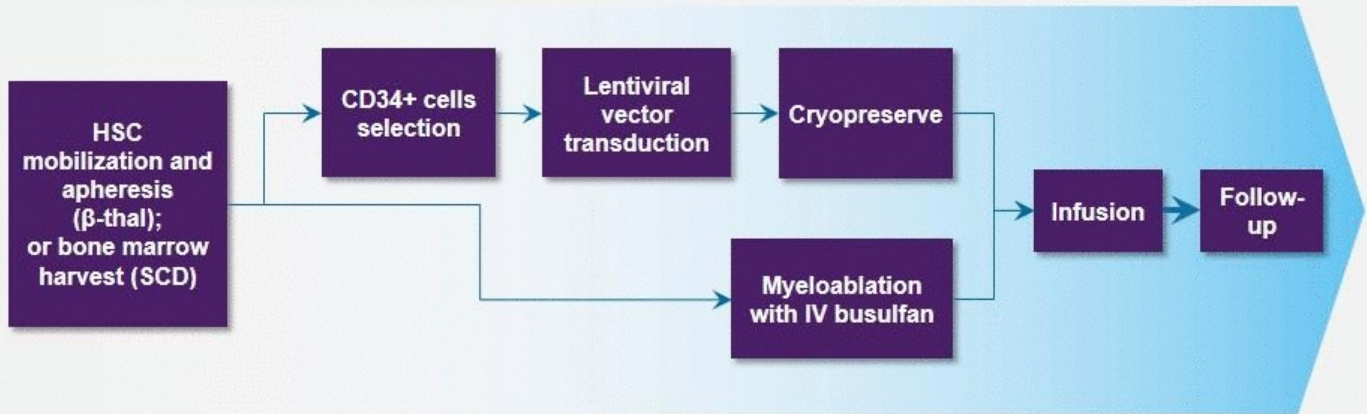
#### **Beta-thalassemia:**

- As of May 2015, beta-thalassemia major Subjects 1201 and 1202 remained transfusion independent for 16 and 14 months, respectively

#### **Sickle Cell Disease:**

- First-ever patient with severe sickle cell disease treated with gene therapy
- Six-month visit post-drug product infusion: proportion of anti-sickling hemoglobin (HbA<sup>T87Q</sup> + HbF) accounted for 45% of all hemoglobin production (40% HbA<sup>T87Q</sup> + 5% HbF)
- No hospitalizations for sickle cell complications post-transplant, despite weaning off transfusions

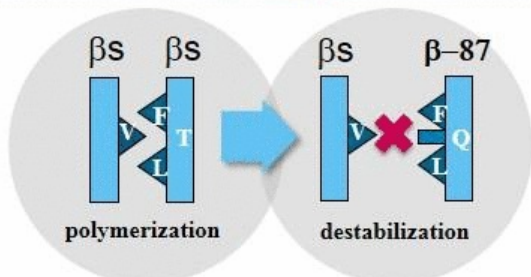
# HGB-205 Study Design



<b>β-thalassemia major</b>	<b>Severe sickle cell disease</b>
Ages 5-35	Ages 5-35
Eligible to undergo HSCT, no matched related donor	Eligible to undergo HSCT, no matched related donor
≥ 100 mL pRBCs/kg/year transfusion requirement	Poor prognostic risk factors (e.g., multiple pain crises, acute chest syndrome, stroke, joint osteonecrosis, alloimmunization)
	Hydroxyurea treatment failed

# Rationale for the Treatment of SCD with BB305 Gene Therapy

## Treatment of SCD by BB305 gene therapy



- HbA<sup>T87Q</sup> incorporates anti-sickling amino acid found in fetal hemoglobin (Takekoshi & Leboulch, PNAS 1995)
- HbA<sup>T87Q</sup> and HbF are more potent inhibitors of HbS polymerization compared to HbA
- Proof of principle in SCD mouse models by Leboulch lab (Pawliuk, Science 2001)

## Data representing hurdle for success

- Patients with SCD and hereditary persistence of fetal hemoglobin with HbF of 30% are typically asymptomatic despite HbS of 70%
- Patients with SCD are asymptomatic after allo-HSCT even with mixed donor chimerism of 15-20%
- While hydroxyurea is not curative, its use can significantly decrease the acute symptoms of SCD when patients are able to achieve and sustain an increase in HbF to >15-20%

**These data suggest that a minimum of 30% anti-sickling hemoglobin (HbA<sup>T87Q</sup> + HbF) could provide disease-modifying clinical benefit**

## Demographics and Baseline Characteristics for Treated Patients with $\beta$ -thalassemia Major and Severe SCD

TRIAL	HGB-205		
	Beta-thalassemia Major		Severe SCD
Disease			
Patient	1201	1202	1204
Age/Sex	18/F	16/M	13/M
Country of birth	Syria	France	France
Genotype	$\beta^0/\beta^E$	$\beta^0/\beta^E$	$\beta^S/\beta^S$
pRBC Transfusion requirement (mls/kg/year) <sup>a</sup> in drug substance	139	188	170
CD34+ VCN (pre-infusion) <sup>b</sup> in drug substance	1.5	2.1	1.2/1.0 <sup>c</sup>
CD34+ cell count ( $\times 10^6/\text{kg}$ )	8.9	13.6	5.6
HbA <sup>T87Q</sup> /total Hb (g/dL) at last visit	7.3/10.5	9.7/12.8	4.3/10.6
Follow-up (months) <sup>d</sup>	15	15	6

<sup>a</sup> mean pRBC requirement per year, over the past 2 years prior to consent

<sup>b</sup> VCN= number of vector copies per diploid genome

<sup>c</sup> If more than one drug substance was manufactured for a subject, the VCN of each drug substance lot is quantified and the cell count is combined

<sup>d</sup> Last scheduled study visit for which results were available as of May 2015

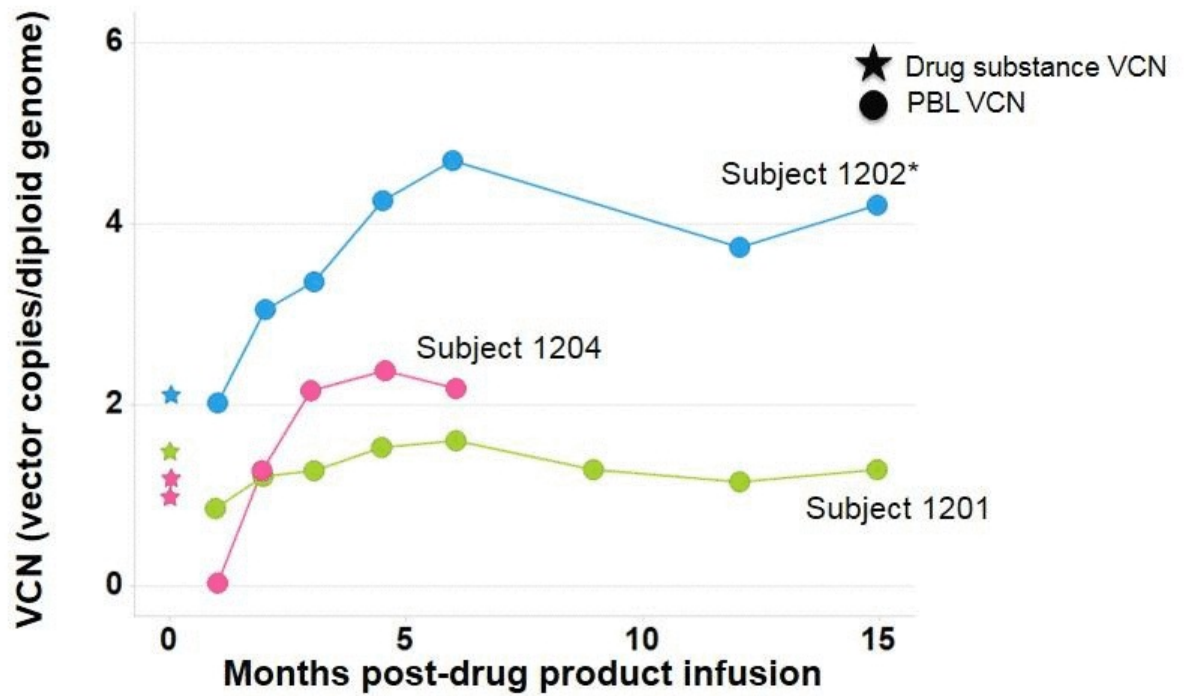


# Clinical Safety for Infused Subjects

Disease	Beta-thalassemia Major		Severe SCD
	1201	1202	1204
Neutrophil engraftment	Day + 13	Day + 15	Day + 37
Platelet engraftment	Day + 17	Day + 24	Day + 91
Non-laboratory $\geq$ Grade 3 AEs	<ul style="list-style-type: none"> <li>• Mucositis</li> <li>• Premature menopause</li> <li>• Herpetic gingivostomatitis</li> </ul>	Mucositis	None
SAEs post-infusion	Grade 3 wisdom tooth infection	None	None

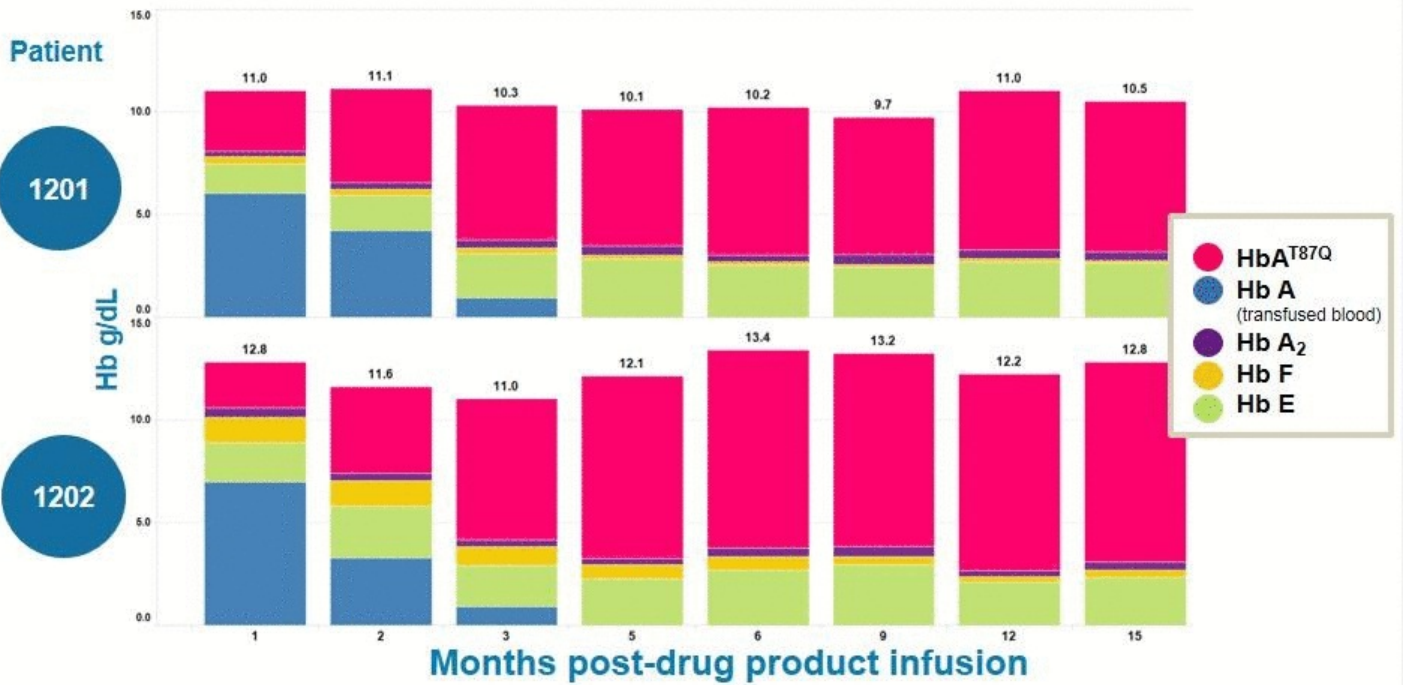
- As of May 18, 2015
- All AEs consistent with myeloablative conditioning
  - No AEs related to drug product
  - No  $\geq$ Grade 3 AEs after day 90 except wisdom tooth infection
  - No replication competent lentivirus (RCL) detected to date
  - Platelet engraftment defined as unsupported platelet count above 50,000 for subjects with SCD; 20,000 for subjects with beta thalassemia

# High and Persistent Levels of Integrated Virus in Peripheral Blood Leukocytes



\*Subject 1202 nine month data not reported due to a sample-specific assay performance issue

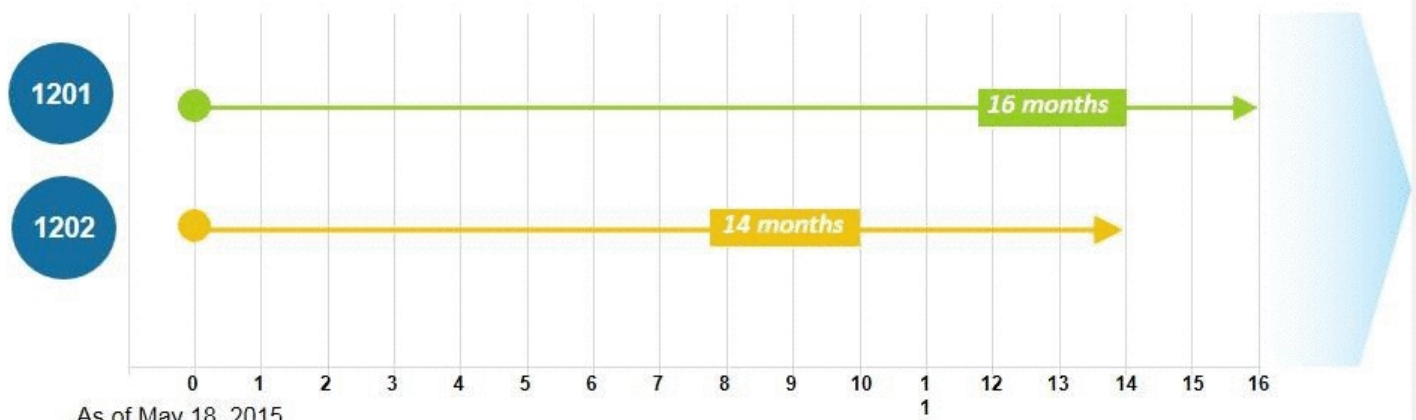
# Sustained High Production of HbA<sup>T87Q</sup> in Both Subjects with $\beta$ -thalassemia Major



Subject 1201 (female) producing 7.3 g/dL HbA<sup>T87Q</sup> at 15 months  
 Subject 1202 (male) producing 9.7 g/dL HbA<sup>T87Q</sup> at 15 months

# Transfusion Independence Sustained for More than One Year

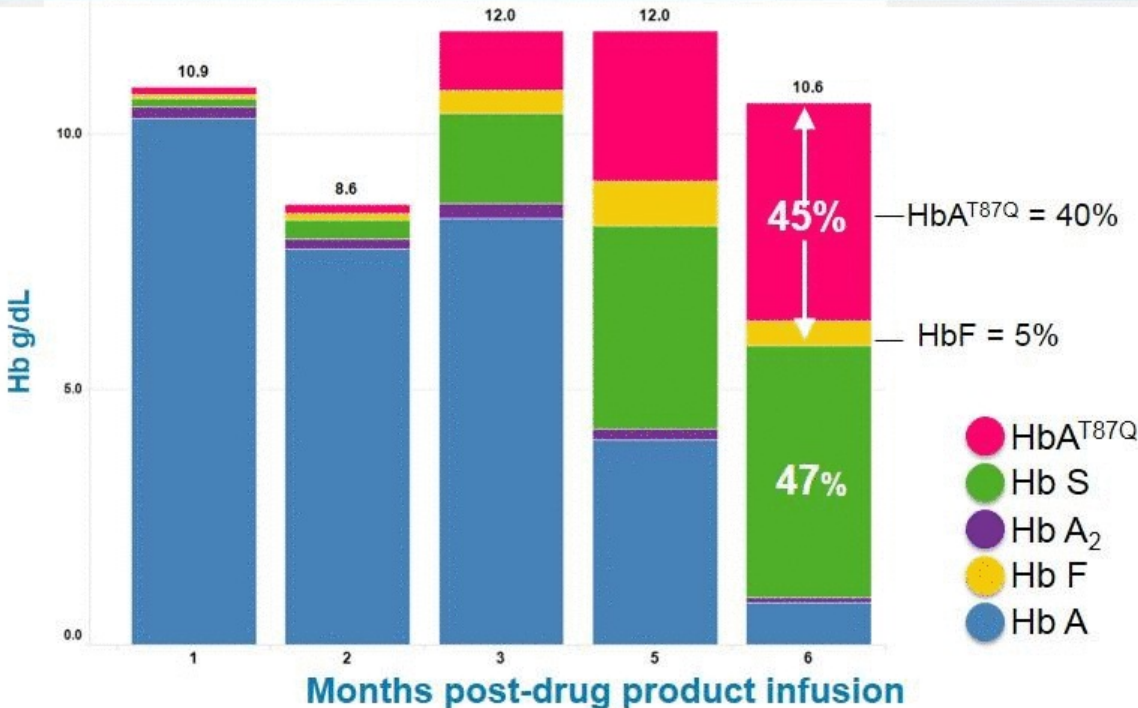
## Months Post-drug Infusion



As of May 18, 2015

- Both 1201 and 1202 show stability or improvements in markers of dyserythropoiesis - LDH, reticulocyte count and erythroblast counts
- Both 1201 and 1202 show improvements in serum ferritin. Only 1201 has follow up liver MRI available and demonstrates improvement in liver iron content (250  $\mu\text{M/g}$  to 200  $\mu\text{M/g}$  from baseline to Month 12)

# Anti-sickling Hemoglobin (HbA<sup>T87Q</sup> + HbF) Accounts for 45% of Total Hemoglobin at Six Months

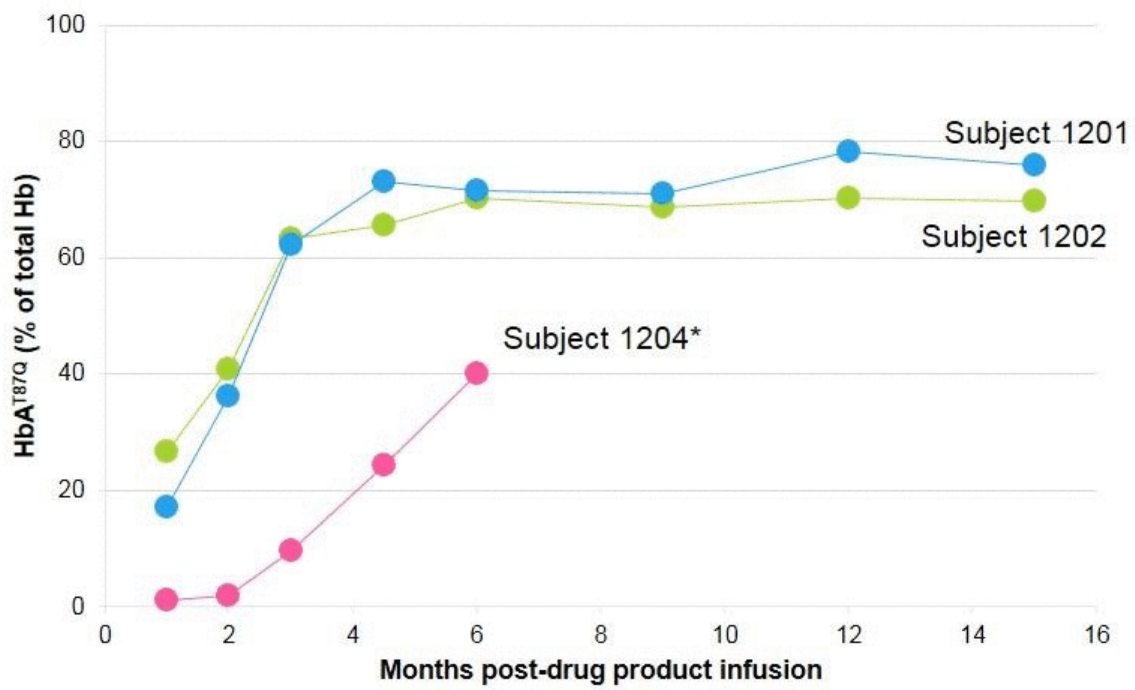


Subject 1204 ( $\beta^S/\beta^S$ ) producing 4.3 g/dL HbA<sup>T87Q</sup> (40%), 0.49 g/dL of HbF (5%) and 4.9 g/dL HbS (47%) at 6 months

# Clinical Outcomes of Subject with Severe SCD

Pre-Transplant (Screening)		Post-Transplant 6M visit
Transfusion History	On chronic transfusions to maintain HbS <30%	Weaned off transfusions; last transfusion on Day + 88 (> 3 months ago)
Hospitalization History	Multiple hospitalizations for VOC prior to beginning transfusion regimen	No hospitalizations or acute SCD-related events since LentiGlobin BB305 Drug Product infusion
Reticulocyte count	238.3 x 10 <sup>9</sup> /L	131.7 x 10 <sup>9</sup> /L
LDH (normal 125-243 U/L)	626 U/L	254 U/L
<ul style="list-style-type: none"> <li>Improvements in markers of hemolysis</li> </ul>		<ul style="list-style-type: none"> <li>No hospitalization for sickle cell complications post-transplant, despite weaning of transfusions</li> </ul>

# HbA<sup>T87Q</sup> Increase in Subjects with Severe SCD and $\beta$ -thalassemia Major



\*Subject 1204 engrafted 3 weeks later than subjects 1201 and 1202

## Additional Update: First Sickle Cell Disease Patient Infused in HGB-206

**HGB-206  
Study  
N=8**

**Patients with severe sickle cell disease  
Open label, multi-center, U.S.-based study**

### Primary & Secondary Endpoints

- Safety and efficacy among patients with severe SCD, as measured by changes in red cell function tests and hemolysis markers
- Clinical events secondary to SCD, including vaso-occlusive crises or acute chest syndrome events

### Status

- Open for enrollment
- Initial data expected in 2015



## Ongoing Studies Using LentiGlobin BB305 Drug Product Worldwide

Study	Centers	Indication	Planned subjects	Current Status
<b>HGB-205</b> (trial reported today)	1 in France	$\beta$ -thalassemia major and severe sickle cell disease	7	7 subjects enrolled 3 subjects treated
<b>HGB-204</b> "Northstar Study"	4 in US 1 in Australia 1 in Thailand	$\beta$ -thalassemia major	18	22 subjects enrolled 10 subjects treated
<b>HGB-206</b>	3-6 planned, all in US	Severe sickle cell disease	8	5 subjects enrolled 1 subject treated

As of June 9, 2015

## Recent Events and Milestones

- ✓ Accelerated regulatory pathway for LentiGlobin in  $\beta$ -thalassemia defined for U.S. and EU
- ✓ Achieved enrollment targets in Starbeam Study (CCALD) and Northstar Study ( $\beta$ -thalassemia major)
- ✓ Defined oncology strategy – BCMA 1<sup>st</sup> CAR T Program; Five Prime target; bluebird independent pathway
- ✓ Presented first SCD data at EHA (Abstract 5/18; EHA presentation 6/13); infused 1<sup>st</sup> patient in HGB-206
- ✓ Appointed Philip Gregory, D.Phil., as Chief Scientific Officer



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