bluebird bio, Inc.
Form 424B5
December 07, 2016
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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-197192

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered(1)	Proposed Maximum Offering Price Per Unit	Proposed Maximum Aggregate Offering Price	Amount of Registration Fee(2)
Common Stock, par value $0.01 per share	3,782,893	$76.00	$287,499,868	$33,321.23

(1) Includes 493,420 shares of common stock, par value $0.01 per share, which may be purchased by the underwriters upon exercise of the underwriters option to purchase additional shares.
(2) Calculated in accordance with Rule 456(b) and 457(r) of the Securities Act of 1933, as amended.

PROSPECTUS SUPPLEMENT

(To prospectus dated July 2, 2014)

3,289,473 Shares

Common Stock

We are selling 3,289,473 shares of our common stock in this offering.

Our common stock is quoted on the NASDAQ Global Select Market under the symbol BLUE. On December 6, 2016, the last reported sale price of our common stock was $78.95 per share, as reported on the NASDAQ Global Select Market.

Investing in our common stock involves risks. See Risk Factors beginning on page S-12 of this prospectus supplement and in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, which is incorporated herein by reference.

Neither the Securities and Exchange Commission nor any other regulatory body has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

We expect that Celgene Corporation, our strategic collaboration partner, will purchase approximately $50 million of shares of our common stock in this offering at the public offering price and on the same terms as the other purchasers in this offering. The underwriters will receive the same underwriting discount on any shares purchased by Celgene as they will on any other shares sold to the public in this offering.

	Per Share	Total
Public offering price	$ 76.00	$ 249,999,948
Underwriting discounts and commissions	$ 4.56	$ 14,999,997
Proceeds, before expenses, to bluebird bio, Inc.	$ 71.44	$ 234,999,951

The underwriters have the option to purchase up to 493,420 additional shares from us at the initial price to public less the underwriting discount.

The underwriters expect to deliver the shares against payment in New York on December 12, 2016.

Goldman, Sachs & Co. **BofA Merrill Lynch** **Cowen and Company**

Wells Fargo Securities **Wedbush PacGrow**

Prospectus supplement dated December 6, 2016.

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We have not authorized anyone to provide any information or to make any representations other than those contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectuses we have prepared. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus is an offer to sell only the shares offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. The information contained in this prospectus supplement and the accompanying prospectus is current only as of its date.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is part of the registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process and consists of two parts. The first part is this prospectus supplement, including the documents incorporated by reference, which describes the specific terms of this offering. The second part, the accompanying prospectus, including the documents incorporated by reference, gives more general information, some of which may not apply to this offering. Generally, when we refer to the prospectus, we are referring to both parts combined. This prospectus supplement may add to, update or change information in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement or the accompanying prospectus.

If information in this prospectus supplement is inconsistent with the accompanying prospectus or with any document incorporated by reference that was filed with the SEC before the date of this prospectus supplement, you should rely on this prospectus supplement. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into each include important information about us, the securities being offered and other information you should know before investing in our securities. You should also read and consider information in the documents we have referred you to in the sections of this prospectus supplement and the accompanying prospectus entitled Where You Can Find Additional Information and Incorporation of Certain Information by Reference.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We take no responsibility for, and can provide no assurances as to the reliability of, any information that is in addition to or different from that contained or incorporated by reference in this prospectus supplement and the accompanying prospectus. We are not offering to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained or incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than as of the date of this prospectus supplement or the accompanying prospectus, as the case may be, or in the case of the documents incorporated by reference, the date of such documents regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or any sale of our securities. Our business, financial condition, liquidity, results of operations and prospects may have changed since those dates.

All references in this prospectus supplement or the accompanying prospectus to bluebird bio, the Company, we, us, our mean bluebird bio, Inc. and our subsidiaries, unless we state otherwise or the context otherwise requires. We use Lenti-D and the bluebird bio logo as trademarks in the United States and other countries. We use and have registered LentiGlobin and bluebird bio in the United States. This prospectus supplement and the information incorporated herein by reference contain references to trademarks, service marks and trade names owned by us or other companies. Solely for convenience, trademarks, service marks and trade names referred to in this prospectus supplement and the information incorporated herein, including logos, artwork, and other visual displays, may appear without the ® or symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, service marks and trade names. We do not intend our use or display of other companies trade names, service marks or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or any related free writing

prospectus are the property of their respective owners.

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No action is being taken in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

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WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act of 1933, as amended, or the Securities Act, with respect to the common stock offered by this prospectus supplement. This prospectus supplement, filed as part of the registration statement, does not contain all the information set forth in the registration statement and its exhibits and schedules, portions of which have been omitted as permitted by the rules and regulations of the SEC. For further information about us, we refer you to the registration statement and to its exhibits and schedules.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy any materials we file at the SEC s Public Reference Room at 100F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information about the Public Reference Room. The SEC also maintains a website at www.sec.gov that contains periodic and current reports, proxy and information statements, and other information regarding registrants that are filed electronically with the SEC.

These documents are also available, free of charge, through the Investors section of our website, which is located at www.bluebirdbio.com. Information contained on our website is not incorporated by reference into this prospectus supplement or the accompanying prospectus and you should not consider information on our website to be part of this prospectus supplement or the accompanying prospectus.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement and the accompanying prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement incorporates by reference the documents listed below (File No. 001-35966) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of this prospectus supplement and the termination of this offering:

- Annual Report on Form 10-K for the year ended December 31, 2015, as filed with the SEC on February 25, 2016;

- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2015 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 21, 2016;

- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2016, June 30, 2016 and September 30, 2016, as filed with the SEC on May 4, 2016 (including the amendment filed with the SEC on November 2, 2016), August 3, 2016 and November 2, 2016, respectively;

Current Reports on Form 8-K filed on February 11, 2016, February 17, 2016, February 25, 2016 (as amended on March 15, 2016), March 3, 2016, April 18, 2016, April 20, 2016 (solely with respect to Item 8.01 and the associated Item 9.01), May 9, 2016, June 3, 2016, September 8, 2016, September 21, 2016, September 29, 2016, October 5, 2016, October 13, 2016, November 3, 2016, November 14, 2016, December 1, 2016 (solely with respect to Item 8.01 and the associated Item 9.01), December 2, 2016 and December 6, 2016; and

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The description of our common stock contained in our registration statement on Form 8-A, which was filed with the SEC on June 14, 2013, including any amendment or report filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by contacting us, either orally or in writing, at the following:

bluebird bio, Inc.

150 Second Street

Cambridge MA 02141

Phone: (617) 245-2107

investor@bluebirdbio.com

Attn: Investor Relations

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated herein by reference herein and therein contain statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These forward-looking statements contain projections of our future results of operations or of our financial position or state other forward-looking information. In some cases you can identify these statements by forward-looking words such as anticipate, believe, could, continue, estimate, expect, intend, may, sho projected or the negative of such words or other similar words or phrases. We believe that it is important to communicate our future expectations to our investors. However, there may be events in the future that we are not able to accurately predict or control and that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements.

Investors are cautioned not to unduly rely on forward-looking statements because they relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- 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;
- our ability to advance our viral vector and drug product manufacturing capabilities;
- the timing or likelihood of regulatory filings and approvals for our product candidates;
- the timing or success of commercialization of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;

- estimates of our expenses, future revenues, capital requirements and our needs for additional financing;
- the potential benefits of strategic collaboration agreements and our ability to enter into strategic arrangements;
- our ability to maintain and establish collaborations and licenses;
- our financial performance;
- developments relating to our competitors and our industry; and
- other risks and uncertainties, including those listed under the caption Risk Factors below and in any documents incorporated by reference herein.

Given these uncertainties, readers should not place undue reliance on our forward-looking statements. These forward-looking statements speak only as of the date on which the statements were made and are not guarantees of future performance. Except as may be required by applicable law, we do not undertake or intend to update any forward-looking statements after the date of this prospectus supplement or the respective dates of documents incorporated by reference herein or therein that include forward-looking statements.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary may not contain all the information that you should consider before investing in our securities. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our common stock discussed under Risk Factors beginning on page S-12 of this prospectus supplement, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus, before making an investment decision. This prospectus supplement may add to, update or change information in the accompanying prospectus.

Overview

We are a clinical-stage biotechnology company committed to developing potentially transformative gene therapies for severe genetic diseases and cancer. With our lentiviral-based gene therapy and gene editing capabilities, we have built an integrated product platform with broad potential application in these areas. We believe that gene therapy for severe genetic diseases has the potential to change the way these patients are treated by correcting the underlying genetic defect that is the cause of their disease, rather than offering treatments that only address their symptoms. We and our scientific collaborators have generated what we believe is human proof-of-concept data for our gene therapy platform in three underserved diseases.

We are conducting four clinical studies of our LentiGlobin product candidate: a Phase I/II study in the United States, Australia, and Thailand, called the Northstar Study, for the treatment of transfusion-dependent ß-thalassemia, or TDT; a global, multi-center Phase III study called the Northstar-2 Study, for the treatment of patients with TDT who do not have a $ß^0/ß^0$ genotype; a single-center Phase I/II study in France (HGB-205) for the treatment of TDT and severe sickle cell disease, or severe SCD; and a Phase I study in the United States (HGB-206) for the treatment of severe SCD. We have achieved our enrollment target of 18 patients in the Northstar Study. Both TDT and severe SCD are rare, hereditary blood disorders that often lead to severe anemia and shortened lifespans. Our LentiGlobin product candidate has been granted Orphan Drug status by the U.S. Food and Drug Administration, or FDA, and the European Medicines Agency, or EMA, for both ß-thalassemia and SCD. Our LentiGlobin product candidate was granted Fast-Track designation by the FDA for the treatment of ß-thalassemia major in January 2013 and for the treatment of certain patients with severe SCD in May 2014. In January 2015, the FDA granted Breakthrough Therapy designation to our LentiGlobin product candidate for the treatment of transfusion-dependent patients with ß-thalassemia major. In September 2016, the EMA has granted access to its Priority Medicines (PRIME) scheme for our LentiGlobin product candidate for the treatment of TDT. Also in September 2016, we initiated our NorthStar-2 Study, which we expect will enroll approximately 15 adult and adolescent patients with TDT who do not have a $ß^0/ß^0$ genotype, with an additional pediatric cohort of up to eight patients for a total enrollment of approximately 23 patients. We expect to evaluate the patients for 24 months following treatment, and anticipate that the primary endpoint of this study will be 12 consecutive months of transfusion independence in the 24 month period following treatment. We have discussed with the FDA and EMA the design of our planned Phase III study (HGB-212) of our LentiGlobin product candidate for patients with TDT who have a $ß^0/ß^0$ genotype, and we anticipate that the primary endpoint of this study will be transfusion reduction.

We are also conducting a Phase II/III clinical study, called the Starbeam Study, of our Lenti-D product candidate, to evaluate its safety and efficacy in subjects with cerebral adrenoleukodystrophy, or CALD, a rare, hereditary neurological disorder that is often fatal. In October 2013, we announced that the first subject had been treated in this study and in May 2015 we announced the achievement of enrollment of 18 subjects in this study. In April 2016, we

announced that, as of March 31, 2016, 17 patients had received Lenti-D drug product, all of which had at least six months of follow up, with eight patients having between 12 and 24 months of follow up. In

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December 2016, we announced that we intend to expand the Starbeam study by 8 additional patients in an effort 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. We plan to begin treating such additional patients in early 2017. We are also conducting an observational study of subjects with CALD treated by allogeneic hematopoietic stem-cell transplant referred to as the ALD-103 study. Our Lenti-D product candidate has been granted Orphan Drug status by the FDA and the EMA for the treatment of adrenoleukodystrophy. If Lenti-D shows a sufficiently compelling treatment effect, and pending further discussion with regulatory authorities, the results from the Starbeam study could potentially form the basis of a BLA and a MAA submission in the United States and European Union, respectively. There can be no assurance that the FDA and the EMA will not require additional studies before the approval of a BLA or MAA, respectively.

Collaboration with Celgene Corporation and bb2121, Our T Cell-based Immunotherapy Program

In March 2013, we entered into a global strategic collaboration with Celgene Corporation, or Celgene, to discover, develop and commercialize chimeric antigen receptor-modified T cells, or CAR T cells, as potentially disease-altering therapies in oncology. This collaboration had an initial term of three years, and Celgene made a $75.0 million up-front, non-refundable cash payment to us as consideration for entering into the collaboration. In June 2015, we amended and restated the collaboration agreement, or the Amended Collaboration Agreement, to focus exclusively on anti-BCMA product candidates for a new three-year term. B-cell maturation antigen, or BCMA, is a cell surface protein that is expressed on normal plasma cells and on most multiple myeloma cells, but is absent from other normal tissues. In February 2016, we treated the first subject in our Phase I clinical study of bb2121, the first anti-BCMA product candidate from this collaboration. This study will enroll up to 50 patients who have received at least three prior regimens for treatment of multiple myeloma. In February 2016, Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb2121. We may elect to co-develop and co-promote bb2121, and any other product candidates in the United States under this collaboration agreement. In May 2016, the FDA granted Orphan Drug status to our bb2121 product candidate for the treatment of relapsed/refractory multiple myeloma.

Gene Editing Technologies

In June 2014, we acquired Precision Genome Engineering, Inc., or Pregenen, a privately-held biotechnology company headquartered in Seattle, Washington. Through the acquisition, we obtained rights to Pregenen s gene editing and cell signaling technology, and have integrated these technologies and research team and expanded our related gene editing discovery research efforts. We are focused on utilizing homing endonuclease and megaTAL gene editing technologies in a variety of potential applications and disease areas, including for severe genetic and rare diseases and oncology. Homing endonucleases and MegaTALs are novel enzymes that provide a highly specific and efficient way to silence, edit or insert genetic components into a cell to potentially treat a variety of diseases.

Risks Related to Our Business

We are a clinical-stage biotechnology company, and our business and ability to execute our business strategy are subject to a number of risks of which you should be aware before you decide to buy our common stock. In particular, you should consider the following risks, which are discussed more fully in the section entitled Risk Factors in this prospectus supplement and in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2016, which are incorporated herein by reference:

We have incurred significant losses since our inception, which we anticipate will continue for the foreseeable future. We have never generated revenue from product sales and may never be profitable.

Failure to obtain additional funding when needed may force us to delay, limit or terminate our product development efforts or other operations.

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Our gene therapy product candidates are based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval.

We may find it difficult to enroll patients in our clinical studies, which could delay or prevent clinical studies of our product candidates.

If our product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our product candidates.

To date, no gene therapy products have been approved in the United States and only a few gene therapy products have been approved in the European Union.

We have not completed any clinical studies of our current viral vectors or product candidates derived from these viral vectors and initial success in our ongoing clinical studies may not be indicative of results obtained when these studies are completed. Furthermore, success in early clinical studies may not be indicative of results obtained in later studies.

Patients with different genotypes may respond differently to treatment with our product candidates, which may result in the delay of our clinical development and commercialization plans.

The results from our Starbeam Study may not be sufficiently robust to support the submission of marketing approval for our Lenti-D product candidate. Before we submit our Lenti-D product candidate for marketing approval, the FDA and the EMA may require us to enroll additional subjects, conduct additional studies, or evaluate subjects for an additional follow-up period.

We cannot be certain that our Northstar-2 clinical study in patients with TDT who do not have a $ß^0/ß^0$ genotype, or our planned Phase III clinical study in patients with TDT who have a $ß^0/ß^0$ genotype, together with data from our Northstar and HGB-205 clinical studies, will be sufficient to form the basis for a BLA submission for our LentiGlobin product candidate.

There can be no assurance that we will ultimately receive conditional marketing approval of our LentiGlobin product candidate in the European Union, or the nature of the conditions that would be imposed on us if conditionally approved.

Changes in our manufacturing processes may cause delays in our clinical development and commercialization plans.

In previous clinical studies involving viral vectors for gene therapy, some subjects experienced serious adverse events, including the development of leukemia due to vector-related insertional oncogenesis. If our vectors demonstrate a similar effect, we may be required to halt or delay further clinical development of our product candidates.

In previous clinical studies involving T cell-based immunotherapies, some subjects experienced serious adverse events. Our T cell-based immunotherapy product candidates may demonstrate a similar effect or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

We expect to rely on third parties to conduct some or all aspects of our vector production, drug product manufacturing, research and preclinical and clinical testing. If they fail to meet deadlines or to perform in a satisfactory manner, our business could be harmed.

We expect to rely on third parties to conduct, supervise and monitor our clinical studies, and if these third parties fail to perform in a satisfactory manner, our business could be harmed.

The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

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If we are unable to obtain or protect intellectual property rights related to our product candidates, we may not be able to compete effectively in our markets.

Company Information

We were incorporated in Delaware in April 1992 under the name Genetix Pharmaceuticals, Inc., and subsequently changed our name to bluebird bio, Inc. in September 2010.

Our mailing address and executive offices are located at 150 Second Street, Cambridge, Massachusetts and our telephone number at that address is (339) 499-9300. We maintain an Internet website at the following address: www.bluebirdbio.com. The information on, or that can be accessed through, our website does not constitute part of this prospectus supplement or the accompanying prospectus, and you should not rely on any such information in making the decision whether to purchase our common stock.

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THE OFFERING

Common stock offered by us	3,289,473 shares. We have also granted the underwriters a 30-day option to purchase up to 493,420 additional shares.
Common stock outstanding following the offering	40,585,076 shares (or 41,078,496 shares if the underwriters exercise their option to purchase additional shares in full).
Use of proceeds	The net proceeds from this offering will be approximately $234.7 million (or approximately $269.9 million if the underwriters exercise their option to purchase additional shares in full), based on the public offering price of $76.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses. We intend to use the net proceeds from this offering to advance the further development of our bb2121 product candidate for multiple myeloma in future trials, as well as the initiation of a Phase I clinical study for an additional anti-BCMA product candidate for the treatment of multiple myeloma; to fund the potential exercise of our option to co-develop and co-promote our bb2121 product candidate, which has been exclusively licensed by Celgene in the United States following the completion of the ongoing Phase I clinical study; to initiate HGB-212, our planned Phase III clinical study of our LentiGlobin product candidate in patients with TDT who have a $ß^0/ß^0$ genotype; to expand our manufacturing capabilities to support both our ongoing and anticipated product development efforts and in anticipation of a potential commercial launch; and to build our commercial infrastructure to support conditional commercial launch of LentiGlobin in Europe pending marketing authorization by the EMA, and for general and administrative expenses, potential future development programs and early-stage research and development, capital expenditures and working capital and other general corporate purposes.
NASDAQ Global Select Market Symbol	BLUE
Risk factors	Investing in our securities involves risks. See Risk Factors beginning on page S-12 of this prospectus supplement and other information included or incorporated by reference into this prospectus supplement and the accompanying prospectus for a discussion of the factors you should carefully consider before deciding to invest in our securities.

We expect that Celgene Corporation, our strategic collaboration partner, will purchase approximately $50 million of shares of our common stock in this offering at the public offering price and on the same terms as the other purchasers in this offering.

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The number of shares of our common stock to be outstanding after the offering is based on 37,295,603 shares of common stock outstanding as of September 30, 2016, and excludes:

- 3,867,113 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2016, at a weighted average exercise price of $51.74 per share;
- 254,200 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2016;
- 1,215,796 shares of common stock reserved for future issuance under our 2013 Stock Option and Incentive Plan, or the 2013 Plan, as of September 30, 2016, plus any future increases in the number of shares of common stock reserved for issuance under the 2013 Plan pursuant to the evergreen provision of the 2013 Plan; and
- 209,117 shares of common stock reserved for future issuance under our 2013 Employee Stock Purchase Plan as of September 30, 2016.

Except as otherwise indicated, all information in this prospectus supplement assumes:

- no exercise by the underwriters of their option to purchase up to 493,420 additional shares of common stock in this offering; and
- no exercise of stock options after September 30, 2016.

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RISK FACTORS

Investing in our securities involves a high degree of risk. In addition to the other information contained in this prospectus supplement, the accompanying prospectus and in the documents we incorporate by reference, you should carefully consider the risks discussed below and under the heading Risk Factors in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, filed with the SEC on November 2, 2016, before making a decision about investing in our securities. The risks and uncertainties discussed below and in our Annual Report on Form 10-K for the fiscal year ended December 31, 2015 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016 are not the only ones facing us. Additional risks and uncertainties not presently know to us, or that we currently see as immaterial, may also harm our business. If any of these risks occur, our business, financial condition and operating results could be harmed, the trading price of our common stock could decline and you could lose part or all of your investment.

Risks Related to this Offering and Our Common Stock

The price of our common stock historically has been volatile, which may affect the price at which you could sell the common stock.

The market price for our common stock has varied between a high price of $79.70 on December 6, 2016 and a low price of $35.37 on May 12, 2016 in the twelve-month period ending on December 6, 2016. This volatility may affect the price at which you could sell the common stock. Our stock price is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market and other factors, including the other factors discussed in our Annual Report on Form 10-K for the year ended December 31, 2015, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2016 or in future periodic reports; variations in our quarterly operating results from our expectations or those of securities analysts or investors; downward revisions in securities analysts estimates; and announcement by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments.

We have broad discretion in the use of the net proceeds from this offering and our existing cash and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled Use of Proceeds, as well as our existing cash, and you will be relying on the judgment of our management regarding such application. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. Our management might not apply the net proceeds or our existing cash in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering or our existing cash in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline. Pending their use, we may invest the net proceeds from this offering in short-term, investment- grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the pro forma book value per share of our tangible assets as of September 30, 2016 after subtracting our liabilities. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of $53.96 per share, based on the difference between the public offering price of $76.00 per share and the as adjusted pro forma net

tangible book value per share of our outstanding common stock as of September 30, 2016.

This dilution is due to the substantially lower price paid by our investors who purchased shares prior to this offering as compared to the price offered to the public in this offering, and the exercise of stock options granted

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to our employees. In addition, as of September 30, 2016, options to purchase 3,867,113 shares of our common stock at a weighted average exercise price of $51.74 per share were outstanding. The exercise of any of these options would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation. Further, because we will need to raise additional capital to fund our clinical development programs, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock.

These future issuances of common stock or common stock-related securities, together with the exercise of outstanding options and any additional shares issued in connection with acquisitions, if any, may result in further dilution. For a further description of the dilution that you will experience immediately after this offering, see Dilution.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

In addition, the sale of substantial amounts of our common stock could adversely impact its price. As of September 30, 2016, we had outstanding 37,295,603 shares of our common stock and options to purchase 3,867,113 shares of our common stock (of which 1,850,376 were exercisable as of that date). The sale or the availability for sale of a large number of shares of our common stock in the public market could cause the price of our common stock to decline.

We have agreed that for a period of 60 days after the date of this prospectus supplement, and our directors and executive officers have agreed that for a period of 45 days after the date of this prospectus supplement, subject to specified exceptions, we or they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock. These lock-up periods affect approximately 95,459 shares of our common stock held by our directors and executive officers as of the date of this prospectus supplement. Sales of stock by any of our directors, executive officers or principal stockholders could have a material adverse effect on the trading price of our common stock.

Certain holders of shares of our common stock are entitled to rights with respect to the registration of their shares under the Securities Act. See Description of Capital Stock Registration Rights. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

The market price of our common stock may be adversely affected by market conditions affecting the stock markets in general, including price and trading fluctuations on the NASDAQ Global Select Market.

Market conditions may result in volatility in the level of, and fluctuations in, market prices of stocks generally and, in turn, our common stock and sales of substantial amounts of our common stock in the market, in each case being unrelated or disproportionate to changes in our operating performance. The overall weakness in the economy has recently contributed to the extreme volatility of the markets which may have an effect on the market price of our common stock.

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Risks Related to Our Business

We have not completed any clinical studies of our current product candidates. Initial success in our ongoing clinical studies may not be indicative of results obtained when these studies are completed. Furthermore, success in early clinical studies may not be indicative of results obtained in later studies.

Our current viral vectors and our product candidates first initiated evaluation in human clinical studies in 2013, and we may experience unexpected results in the future. Earlier gene therapy clinical studies, which we believe serve as proof-of-concept for our product candidates, utilized lentiviral vectors similar to ours. However, these studies should not be relied upon as evidence that our ongoing or future clinical studies will succeed. Study designs and results from previous or ongoing studies are not necessarily predictive of our future clinical study results, and initial or interim results may not continue or be confirmed upon completion of the study. There is limited data concerning long-term safety and efficacy following treatment with our gene therapy and CAR-T product candidates. These data, or other positive data, may not continue or occur for these subjects or for any future subjects in our ongoing or future clinical studies, and may not be repeated or observed in ongoing or future studies involving our product candidates. For instance, while patients with TDT or severe SCD who have been treated with our LentiGlobin product candidate may experience a reduction or temporary elimination of transfusion support, there can be no assurance that they will not require transfusion support in the future. Similarly, patients with relapsed/refractory multiple myeloma who have been treated with our bb2121 product candidate may experience disease progression. Furthermore, our product candidates may also fail to show the desired safety and efficacy in later stages of clinical development despite having successfully advanced through initial clinical studies. There can be no assurance that any of these studies will ultimately be successful or support further clinical advancement or regulatory approval of our product candidates.

There is a high failure rate for drugs and biologics proceeding through clinical studies. A number of companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in later stage clinical studies even after achieving promising results in earlier stage clinical studies. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, regulatory delays or rejections may be encountered as a result of many factors, including changes in regulatory policy during the period of product development.

In previous clinical studies involving T cell-based immunotherapies, some subjects experienced serious adverse events. Our T cell-based immunotherapy product candidates may demonstrate a similar effect or have other properties that could halt their clinical development, prevent their regulatory approval, limit their commercial potential, or result in significant negative consequences.

Our bb2121 product candidate is a chimeric antigen receptor, or CAR, T cell-based immunotherapy. In previous and ongoing clinical studies involving CAR T cell products by other companies or academic researchers, many subjects experienced side effects such as neurotoxicity and cytokine release syndrome, which have in some cases resulted in clinical holds in ongoing clinical trials of CAR T product candidates. There have been life threatening events related to severe neurotoxicity and cytokine release syndrome, requiring intense medical intervention such as intubation or pressor support, and in several cases, resulted in death. Severe neurotoxicity is a condition that is currently defined clinically by cerebral edema, confusion, drowsiness, speech impairment, tremors, seizures, or other central nervous system side effects, when such side effects are serious enough to lead to intensive care. In some cases, severe neurotoxicity was thought to be associated with the use of certain lymphodepletion regimens used prior to the administration of the CAR T cell products. Cytokine release syndrome is a condition that is currently defined clinically by certain symptoms related to the release of cytokines, which can include fever, chills, low blood pressure, when such side effects are serious enough to lead to intensive care with mechanical ventilation or significant vasopressor support. The exact cause or causes of cytokine release syndrome and severe neurotoxicity in connection

with treatment of CAR T cell products is not fully understood at this time. In addition, subjects have experienced other adverse events in these studies, such as a reduction in the number of blood cells (in the form of neutropenia, thrombocytopenia, anemia or other cytopenias), febrile neutropenia, chemical laboratory abnormalities (including elevated liver enzymes), and renal failure.

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Undesirable side effects caused by our bb2121 product candidate, other CAR T product candidates targeting BCMA, or our other T cell-based immunotherapy product candidates, could cause us or regulatory authorities to interrupt, delay or halt clinical studies and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign regulatory authorities. Results of our studies could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. Treatment-related side effects could also affect patient recruitment or the ability of enrolled subjects to complete the studies or result in potential product liability claims. In addition, these side effects may not be appropriately recognized or managed by the treating medical staff, as toxicities resulting from T cell-based immunotherapies are not normally encountered in the general patient population and by medical personnel. We expect to have to train medical personnel regarding our T cell-based immunotherapy product candidates to understand their side effects for both our planned clinical trials and upon any commercialization of any T cell-based immunotherapy product candidates. Inadequate training in recognizing or managing the potential side effects of T cell-based immunotherapy product candidates could result in patient deaths. Any of these occurrences may harm our business, financial condition and prospects significantly.

Changes in our manufacturing processes may cause delays in our clinical development and commercialization plans.

The manufacturing processes for our lentiviral vectors and our product candidates are complex. We have developed and are implementing changes in our manufacturing processes for our LentiGlobin product candidate, and drug product manufactured using these changed processes will be administered in our Northstar-2 (HGB-207) clinical study in TDT patients who do not have a $ß^0/ß^0$ genotype, our expanded HGB-206 clinical study in patients with severe SCD and our planned HGB-212 clinical study in TDT patients who have a $ß^0/ß^0$ genotype. There can be no assurances that LentiGlobin drug product manufactured using these new processes will have similar or improved efficacy or safety compared to the LentiGlobin drug product used in the ongoing Northstar (HGB-204), HGB-205 or historical HGB-206 clinical studies.

As we develop a commercial-scale manufacturing process for our LentiGlobin and Lenti-D product candidates, we are implementing improvements to the manufacturing process for both producing our lentiviral vectors and for our product candidates on a continual basis. In some circumstances, changes in the manufacturing process may require us to perform additional comparability studies or to collect additional clinical data from patients prior to undertaking additional clinical studies or filing for regulatory approval. These requirements may lead to delays in our clinical development and commercialization plans.

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USE OF PROCEEDS

The net proceeds from the sale of shares of common stock that we are selling in this offering will be approximately $234.7 million based on the sale of 3,289,473 shares of our common stock offered hereby, or approximately $269.9 million if the underwriters exercise in full their option to purchase up to 493,420 additional shares of common stock at the public offering price of $76.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds of this offering as follows:

- To advance the further development of our bb2121 product candidate for multiple myeloma in future trials, as well as the initiation of a Phase I clinical study for an additional anti-BCMA product candidate for the treatment of multiple myeloma;

- To fund the potential exercise of our option to co-develop and co-promote our bb2121 product candidate, which has been exclusively licensed by Celgene, in the United States following the completion of the ongoing Phase I clinical study;

- To initiate HGB-212, our planned Phase III clinical study of our LentiGlobin product candidate in patients with TDT who have a $ß^0/ß^0$ genotype;

- To expand our manufacturing capabilities to support our ongoing and anticipated product development efforts, and in anticipation of a potential commercial launch; and

- To build our commercial infrastructure to support conditional commercial launch of LentiGlobin in Europe pending marketing authorization in Europe.

We expect to use the remaining net proceeds from this offering for general and administrative expenses (including personnel-related costs), potential future development programs, early-stage research and development, capital expenditures and working capital and other general corporate purposes.

Our expected use of net proceeds from this offering represents our current intentions based upon our present plans and business condition. As of the date of this prospectus supplement, we cannot predict with certainty all of the particular uses for the net proceeds to be received upon the completion of this offering or the amounts that we will actually spend on the uses set forth above. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary gene therapy or immuno-oncology businesses, technologies, products or assets. Due to the many variables inherent to the development of gene therapy products at this time, such as the timing of patient enrollment and evolving regulatory requirements, we cannot currently predict the stage of development we expect the net proceeds of this offering to achieve for our clinical studies and product candidates.

The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our research and development efforts, the timing and success of preclinical studies, our ongoing clinical studies or clinical studies we may commence in the future and the timing of regulatory submissions. As a result, our management will

have broad discretion over the use of the net proceeds from this offering.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities, certificates of deposit or government securities.

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DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the price per share of our common stock in this offering and the as adjusted net tangible book value per share of our common stock immediately after this offering.

As of September 30, 2016, we had net tangible book value of approximately $659.8 million, or $17.69 per share of our common stock, based upon 37,295,603 shares of our common stock outstanding as of that date. Historical net tangible book value per share is equal to our total tangible assets, less total liabilities, divided by the number of outstanding shares of our common stock. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of 3,289,473 shares of common stock in this offering at the public offering price of $76.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2016 would have been approximately $894.5 million, or approximately $22.04 per share of common stock. This represents an immediate increase in as adjusted net tangible book value of $4.35 per share to our existing stockholders and an immediate dilution of $53.96 per share to investors participating in this offering at the public offering price. The following table illustrates this per share dilution:

Public offering price per share		$ 76.00
Historical net tangible book value per share as of September 30, 2016	$ 17.69	
Increase in net tangible book value per share attributable to new investors	4.35	
As adjusted net tangible book value per share after this offering		22.04
Dilution per share to new investors		$ 53.96

The foregoing table and discussion is based on 37,295,603 shares of common stock outstanding as of September 30, 2016, and excludes:

- 3,867,113 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2016, at a weighted average exercise price of $51.74 per share;
- 254,200 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2016;
- 1,215,796 shares of common stock reserved for future issuance under the 2013 Plan as of September 30, 2016; and

209,117 shares of common stock reserved for future issuance under our 2013 Employee Stock Purchase Plan as of September 30, 2016.

If the underwriters exercise in full their option to purchase up to 493,420 additional shares of common stock at the public offering price of $76.00 per share, the as adjusted net tangible book

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value after this offering would be $22.63 per share, representing an increase in net tangible book value of $4.94 per share to existing stockholders and immediate dilution in net tangible book value of $53.37 per share to investors purchasing our common stock in this offering at the public offering price.

To the extent that any options are exercised, new options are issued under our equity incentive plans, or we otherwise issue additional shares of common stock in the future (including shares issued in connection with acquisitions), there will be further dilution to new investors.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

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DESCRIPTION OF CAPITAL STOCK

This section describes the general terms of our common stock. For more detailed information, a holder of our common stock should refer to our certificate of incorporation and our by-laws, copies of which are filed with the SEC as exhibits to the registration statement of which this prospectus supplement and the accompanying prospectus are a part.

General

Our authorized capital stock consists of 125,000,000 shares of common stock, $0.01 par value per share, and 5,000,000 shares of preferred stock, $0.01 par value per share. As of September 30, 2016, there were 37,295,603 shares of our common stock outstanding and no shares of preferred stock were outstanding.

The following summary description of our capital stock is based on the provisions of our amended and restated certificate of incorporation and amended and restated bylaws and the applicable provisions of the Delaware General Corporation Law. This information is qualified entirely by reference to the applicable provisions of our amended and restated certificate of incorporation, amended and restated bylaws and the Delaware General Corporation Law.

Common Stock

Holders of our common stock are entitled to one vote for each share of common stock held of record for the election of directors and on all matters submitted to a vote of stockholders. Holders of our common stock are entitled to receive dividends ratably, if any, as may be declared by our board of directors out of legally available funds, subject to any preferential dividend rights of any preferred stock then outstanding. Upon our dissolution, liquidation or winding up, holders of our common stock are entitled to share ratably in our net assets legally available after the payment of all our debts and other liabilities, subject to the preferential rights of any preferred stock then outstanding. Holders of our common stock have no preemptive, subscription, redemption or conversion rights. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. Except as described below in Anti-takeover effects of Delaware law, our certificate of incorporation and our by-laws, a majority vote of common stockholders is generally required to take action under our certificate of incorporation and by-laws.

Preferred Stock

Pursuant to our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or NASDAQ rules), to designate and issue up to 5,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series, and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

We will fix the rights, preferences and privileges of the preferred stock of each such series, as well as any qualifications, limitations or restrictions thereon, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus supplement and the accompanying prospectus are a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock.

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Registration Rights

Prior to the initial public offering of our common stock, we entered into an amended and restated investors rights agreement with certain of our stockholders of shares of our common stock issuable upon conversion of the shares of preferred stock. Under the amended and restated investors rights agreement, holders of registrable shares can demand that we file a registration statement or request that their shares be included on a registration statement that we are otherwise filing, in either case, registering the resale of their shares of common stock. These registration rights are subject to conditions and limitations, including the right, in certain circumstances, of the underwriters of an offering to limit the number of shares included in such registration and our right, in certain circumstances, not to effect a requested S-1 registration within 60 days before or 180 days following any offering of our securities, including this offering or a requested S-3 registration within 30 days before or 90 days following any offering of our securities, including this offering.

Demand Registration Rights

The holders of registrable shares may require us to file a registration statement under the Securities Act on a Form S-3, if available, at our expense with respect to the resale of their registrable shares, and we are required to use our best efforts to effect the registration.

Piggyback Registration Rights

If we propose to register any of our securities under the Securities Act for our own account or the account of any other holder, the holders of registrable shares are entitled to notice of such registration and to request that we include registrable shares for resale on such registration statement, subject to the right of any underwriter to limit the number of shares included in such registration. The requisite holders have waived registration rights in connection with this offering.

We will pay all registration expenses, other than underwriting discounts and commissions, related to any demand or piggyback registration. The amended and restated investors rights agreement contains customary cross-indemnification provisions, pursuant to which we are obligated to indemnify the selling stockholders, in the event of misstatements or omissions in the registration statement attributable to us except in the event of fraud and they are obligated to indemnify us for misstatements or omissions attributable to them. The registration rights will terminate upon the later of (1) such time as Rule 144 or another similar exemption under the Securities Act is available for the sale of all the registrable shares of a holder during a three-month period without registration, and (2) the fifth anniversary of the closing date of our initial public offering.

Anti-takeover Effects of Delaware Law, our Certificate of Incorporation and our By-Laws

Our certificate of incorporation and by-laws include a number of provisions that may have the effect of encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

In accordance with our certificate of incorporation, our board is divided into three classes serving three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a

vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum.

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No Written Consent of Stockholders

Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

Meetings of Stockholders

Our by-laws provide that only a majority of the members of our board of directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our by-laws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

Advance Notice Requirements

Our by-laws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days or more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. The notice must contain certain information specified in the by-laws. These provisions may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer s own slate of directors or otherwise attempting to obtain control of our company.

Amendment to By-Laws and Certificate of Incorporation

As required by the Delaware General Corporation Law, any amendment of our certificate of incorporation must first be approved by a majority of our board of directors and, if required by law or our certificate of incorporation, thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment, and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, directors, limitation of liability, exclusive jurisdiction of Delaware Courts and the amendment of our by-laws and certificate of incorporation must be approved by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our by-laws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the by-laws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if the board of directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

Blank Check Preferred Stock

Our certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute

the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the

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rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

Section 203 of the Delaware General Corporation Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a business combination with an interested stockholder for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An interested stockholder is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation s voting stock.

Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

A Delaware corporation may opt out of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or by-laws resulting from a stockholders amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Exclusive Jurisdiction of Certain Actions

Our certificate of incorporation requires that, to the fullest extent permitted by law, derivative actions brought in our name, actions against our directors, officers and employees for breach of fiduciary duty and other similar actions may be brought only in the Court of Chancery in the State of Delaware, unless we otherwise consent. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC.

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PRICE RANGE OF COMMON STOCK

Our common stock is listed on the NASDAQ Global Select Market under the symbol BLUE . The following table sets forth the high and low sale prices per share of our common stock as reported by the NASDAQ Global Select Market for the periods indicated:

	Sales prices	
	High	**Low**
Year ended December 31, 2014		
First Quarter	$ 28.08	$ 19.34
Second Quarter	$ 41.75	$ 17.40
Third Quarter	$ 40.31	$ 30.33
Fourth Quarter	$ 94.95	$ 29.73
Year ended December 31, 2015		
First Quarter	$ 128.88	$ 83.00
Second Quarter	$ 197.35	$ 116.00
Third Quarter	$ 171.24	$ 82.05
Fourth Quarter	$ 106.95	$ 48.85
Year ending December 31, 2016		
First Quarter	$ 65.00	$ 37.40
Second Quarter	$ 53.38	$ 35.37
Third Quarter	$ 74.95	$ 43.10
Fourth Quarter (through December 6, 2016)	$ 79.70	$ 37.05

As of September 30, 2016, there were approximately eleven record holders of our common stock. The actual number of stockholders is greater than this number of record holders and includes stockholders who are beneficial owners but whose shares are held in street name by brokers and other nominees.

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DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be made at the discretion of our board of directors.

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UNDERWRITING

We and the underwriters named below have entered into an underwriting agreement with respect to the shares being offered. Subject to certain conditions, each underwriter has severally agreed to purchase the number of shares indicated in the following table. Goldman, Sachs & Co., Merrill Lynch, Pierce, Fenner & Smith Incorporated and Cowen and Company, LLC are the representatives of the underwriters.

Underwriters	Number of Shares
Goldman, Sachs & Co	1,218,324
Merrill Lynch, Pierce, Fenner & Smith Incorporated	1,120,857
Cowen and Company, LLC	706,628
Wells Fargo Securities, LLC	121,832
Wedbush Securities Inc.	121,832
Total	3,289,473

The underwriters are committed to take and pay for all of the shares being offered, if any are taken, other than the shares covered by the option described below unless and until this option is exercised.

The underwriters have an option to buy up to 493,420 additional shares from us. They may exercise that option for 30 days. If any shares are purchased pursuant to this option, the underwriters will severally purchase shares in approximately the same proportion as set forth in the table above.

We expect that Celgene Corporation, our strategic collaboration partner, will purchase approximately $50 million of shares of our common stock in this offering at the public offering price and on the same terms as the other purchasers in this offering. The underwriters will receive the same underwriting discount on any shares purchased by Celgene as they will on any other shares sold to the public in this offering.

The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters by us. Such amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

	Paid by the Company	
	No Exercise	Full Exercise
Per Share	$ 4.56	$ 4.56
Total	$ 14,999,997	$ 17,249,992

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to $2.508 per share from the public offering price. After the initial offering of the shares, the representatives may change the offering price and the other selling terms. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters right to reject any order in whole or in part.

Except with the prior written consent of the representatives, we have agreed with the underwriters that for a period of 60 days after the date of this prospectus supplement, and our directors and executive officers have agreed with the underwriters that for a period of 45 days after the date of this prospectus supplement, not to

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dispose of or hedge any of their common stock or securities convertible into or exchangeable for shares of common stock, subject to certain exceptions. This agreement does not apply to any existing employee benefit plans.

The restrictions described in the immediately preceding paragraph do not apply to directors and executive officers with respect to:

- transfers (1) as a bona fide gift, (2) to a trust or limited family partnership for the direct or indirect benefit of the security holder, or (3) by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the undersigned in a transaction not involving a disposition for value; provided that in each case, each transferee, trustee, donee or distributee shall sign and deliver a lock-up agreement and no filing under Section 16(a) of the Exchange Act reporting a reduction in beneficial ownership of shares of common stock shall be required or shall be voluntarily made during the restricted period;

- transactions relating to shares of common stock acquired in open market transactions after the completion of this offering;

- transfers of common stock pursuant to a trading plan established pursuant to Rule 10b5-1 under the Exchange Act prior to the date hereof, which trading plan shall not be amended, but may be terminated, during the restricted period; and

- the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares of common stock, provided that such plan does not provide for the transfer of common stock during the restricted period.

In addition, the restrictions described above do not apply to us with respect to:

- the shares of common stock to be sold by us in this offering;

- the issuance by us of shares of common stock upon the exercise of an option or warrant;

- the issuance by us of shares or options to purchase shares of common stock pursuant to our equity plans;

- the filing by us of a registration statement on Form S-8 or a successor form thereto; and

- the issuance by us of shares issued in connection with a transaction with an unaffiliated third party that includes a bona fide commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of

assets or not less than a majority or controlling portion of the equity of another entity; provided that the aggregate number of shares issued shall not exceed ten percent of the total number of outstanding shares of our common stock immediately following this offering; provided further that the recipient of any such shares during the 60-day restricted period described above shall enter into an agreement providing for transfer restrictions as set forth above.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A covered short position is a short position that is not greater than the amount of additional shares for which the underwriters option described above may be exercised. The

underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. Naked short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Purchases to cover a short position and stabilizing transactions, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of our stock, and together with the imposition of the penalty bid, may stabilize, maintain or otherwise affect the market price of the common stock. As a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. The underwriters are not required to engage in these activities and may end any of these activities at any time. These transactions may be effected on the Nasdaq Global Select Market, in the over-the-counter market or otherwise.

The Company may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. In connection with those derivatives, the third parties may sell securities covered by this prospectus, including in short sale transactions. If so, the third party may use securities pledged by the Company or borrowed from the Company or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from the Company in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter or will be identified in a post-effective amendment.

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

We estimate that our share of the total expenses of the offering, excluding underwriting discounts and commissions, will be approximately $300,000.

We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to the issuer and to persons and entities with relationships with the issuer, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities,

derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve

or relate to assets, securities and/or instruments of the issuer (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with the issuer. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relative Member State) an offer to the public of our common shares may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of our common shares may be made at any time under the following exemptions under the Prospectus Directive:

To any legal entity which is a qualified investor as defined in the Prospectus Directive;

To fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the representatives for any such offer; or

In any other circumstances falling within Article 3(2) of the Prospectus Directive;

provided that no such offer or shares of our common stock shall result in a requirement for the publication by us or any Brazilian placement agent of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an offer to public in relation to our common shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common shares to be offered so as to enable an investor to decide to purchase our common shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (as amended), including by Directive 2010/73/EU and includes any relevant implementing measure in the Relevant Member State.

This European Economic Area selling restriction is in addition to any other selling restrictions set out below.

United Kingdom

In the United Kingdom, this prospectus is only addressed to and directed as qualified investors who are (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order); or (ii) high net worth entities and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). Any investment or investment activity to which this prospectus relates is available only to relevant persons and will only be engaged with relevant persons. Any person who is not a relevant person should not act or relay on this prospectus or any of its contents.

Canada

The securities may be sold in Canada only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions, and Ongoing Registrant Obligations. Any resale of the securities must be made in accordance with an exemption form, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this offering memorandum (including any amendment thereto) contains a

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misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser s province or territory of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32 of the Laws of Hong Kong) (Companies (Winding Up and Miscellaneous Provisions) Ordinance) or which do not constitute an invitation to the public within the meaning of the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (Securities and Futures Ordinance), or (ii) to professional investors as defined in the Securities and Futures Ordinance and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a prospectus as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance, and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors in Hong Kong as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor (as defined under Section 4A of the Securities and Futures Act, Chapter 289 of Singapore (the SFA)) under Section 274 of the SFA, (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor, the securities (as defined in Section 239(1) of the SFA) of that corporation shall not be transferable for 6 months after that corporation has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer in that corporation s securities pursuant to Section 275(1A) of the SFA, (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore (Regulation 32)

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is a trust (where the trustee is not an accredited investor (as defined in Section 4A of the SFA)) whose sole purpose is to

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hold investments and each beneficiary of the trust is an accredited investor, the beneficiaries rights and interest (howsoever described) in that trust shall not be transferable for 6 months after that trust has acquired the shares under Section 275 of the SFA except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (2) where such transfer arises from an offer that is made on terms that such rights or interest are acquired at a consideration of not less than S$200,000 (or its equivalent in a foreign currency) for each transaction (whether such amount is to be paid for in cash or by exchange of securities or other assets), (3) where no consideration is or will be given for the transfer, (4) where the transfer is by operation of law, (5) as specified in Section 276(7) of the SFA, or (6) as specified in Regulation 32.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Act of Japan (Act No. 25 of 1948, as amended), or the FIEA. The securities may not be offered or sold, directly or indirectly, in Japan or to or for the benefit of any resident of Japan (including any person resident in Japan or any corporation or other entity organized under the laws of Japan) or to others for reoffering or resale, directly or indirectly, in Japan or to or for the benefit of any resident of Japan, except pursuant to an exemption from the registration requirements of the FIEA and otherwise in compliance with any relevant laws and regulations of Japan.

Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market.

Dubai International Financial Centre

This prospectus supplement relates to an Exempt Offer in accordance with the Offered Securities Rules of the Dubai Financial Services Authority, or the DFSA. This prospectus supplement is intended for distribution only to persons of a type specified in the Offered Securities Rules of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for the prospectus supplement. The shares to which this prospectus supplement relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus supplement you should consult an authorized financial advisor.

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MATERIAL U.S. FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following is a summary of the material U.S. federal income tax consequences of the ownership and disposition of our common stock to non-U.S. holders, but does not purport to be a complete analysis of all the potential tax considerations relating thereto. This summary is based upon the provisions of the Internal Revenue Code of 1986, as amended, or the Code, Treasury regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed or subject to differing interpretations, possibly with retroactive effect, so as to result in U.S. federal income tax consequences different from those set forth below. We have not sought any ruling from the Internal Revenue Service, or the IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions.

This summary also does not address the tax considerations arising under the laws of any U.S. state or local or any non-U.S. jurisdiction, the Medicare tax on net investment income or any alternative minimum tax consequences. In addition, this discussion does not address tax considerations applicable to an investor s particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

banks, insurance companies or other financial institutions;

tax-exempt organizations;

dealers in securities or currencies;

traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;

persons that own, or are deemed to own, more than five percent of our capital stock;

certain former citizens or long-term residents of the United States;

persons who hold our common stock as a position in a hedging transaction, straddle, conversion transaction or other risk reduction transaction;

persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes);

persons deemed to sell our common stock under the constructive sale provisions of the Code;

regulated investment companies;

pension plans;

controlled foreign corporations;

passive foreign investment companies; or

persons that acquire our common stock as compensation for services.

In addition, if a partnership, including any entity or arrangement classified as a partnership for U.S. federal income tax purposes, holds our common stock, the tax treatment of a partner generally will depend on the status of the partner and upon the activities of the partnership. Accordingly, partnerships that hold our common stock, and partners in such partnerships, should consult their tax advisors.

You are urged to consult your tax advisor with respect to the application of the U.S. federal income tax laws to your particular situation, as well as any tax consequences of the purchase, ownership and disposition of our common stock arising under the U.S. federal estate or gift tax rules or under the laws of any U.S. state or local or any non-U.S. or other taxing jurisdiction or under any applicable tax treaty.

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Non-U.S. Holder Defined

For purposes of this discussion, you are a non-U.S. holder if you are a beneficial owner of our common stock that is for United States federal income tax purposes (i) a foreign corporation, (ii) a nonresident alien individual, or (iii) a foreign estate or trust that in either case is not subject to U.S. federal income tax on a net- income basis on income or gain from a note or share of common stock.

Distributions

If we make distributions on our common stock, those payments will constitute dividends for U.S. tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, they will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock.

Any dividend paid to you generally will be subject to U.S. withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty. In order to receive a reduced treaty rate, you must provide us with an IRS Form W-8BEN (generally including a U.S. taxpayer identification number), IRS Form W-8-BEN-E or another appropriate version of IRS Form W-8 (or a successor form), in each case, certifying qualification for the reduced rate.

Dividends received by you that are effectively connected with the conduct of a U.S. trade or business (and, if an income tax treaty applies, are attributable to a permanent establishment maintained by you in the United States) generally are exempt from such withholding tax. In order to obtain this exemption, you must provide us with an IRS Form W-8ECI or successor form or other applicable IRS Form W-8 properly certifying such exemption. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits, subject to an applicable income tax treaty providing otherwise. In addition, if you are a corporate non-U.S. holder, dividends you receive that are effectively connected with your conduct of a U.S. trade or business (and, if an income tax treaty applies, are attributable to a permanent establishment maintained by the you in the United States) may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty.

If you are eligible for a reduced rate of withholding tax pursuant to a tax treaty, you may be able to obtain a refund of any excess amounts currently withheld if you file an appropriate claim for refund with the IRS.

Gain on Sale or Other Disposition of Common Stock

Subject to the discussion below regarding backup withholding and FATCA, a non-U.S. Holder generally will not be required to pay U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with the conduct of a U.S. trade or business (and, if an income tax treaty applies, the gain is attributable to a permanent establishment maintained by you in the U.S.), in which case you will be required to pay tax on the net gain derived from the sale under regular graduated U.S. federal income tax rates, and for a non-U.S. holder that is a corporation, such non-U.S. holder may be subject to the branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty;

you are an individual who is present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met, in which case you will be required to pay a flat 30% tax on the gain derived from the sale, which tax may be offset by U.S. source capital losses (even though you are not considered a resident of the United States) (subject to applicable income tax or other treaties); or

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our common stock constitutes a U.S. real property interest by reason of our status as a U.S. real property holding corporation for U.S. federal income tax purposes, a USRPHC, at any time within the shorter of the five-year period preceding the disposition or your holding period for our common stock. We believe that we are not currently and will not become a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, such common stock will be treated as U.S. real property interests only if you actually or constructively hold more than five percent of such regularly traded common stock at any time during the applicable period that is specified in the Code.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address, and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends or of proceeds on the disposition of stock made to you may be subject to additional information reporting and backup withholding at a current rate of 28% unless you establish an exemption, for example by properly certifying your non-U.S. status on an IRS Form W-8BEN, IRS Form W-8BEN-E or another appropriate version of IRS Form W-8 (or a successor form). Notwithstanding the foregoing, backup withholding and information reporting may apply if either we or our paying agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may generally be obtained from the IRS, provided that the required information is furnished to the IRS in a timely manner.

Foreign Account Tax Compliance Act (FATCA)

Provisions commonly referred to as FATCA may impose withholding tax on certain types of payments made to foreign financial institutions and certain other non-U.S. entities. The legislation imposes a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution or to certain non-financial foreign entities, unless (i) the foreign financial institution undertakes certain diligence and reporting obligations or (ii) the non-financial foreign entity either certifies it does not have any substantial U.S. owners or furnishes identifying information regarding each substantial U.S. owner and such entity meets certain other specified requirements. If the payee is a foreign financial institution, it must enter into an agreement with the U.S. Treasury requiring, among other things, that it undertake to identify accounts held by certain U.S. persons or U.S.-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. If the country in which a payee is resident has entered into an intergovernmental agreement with the United States regarding FATCA, that agreement may permit the payee to report to that country rather than to the U.S. Treasury. Under applicable U.S. Treasury regulations, withholding under FATCA may apply to payments of dividends on our common stock, but may only apply to payments of gross proceeds from a sale or other disposition of our common stock made after December 31, 2018. Under certain circumstances, a non-U.S. holder may be eligible for refunds or credits of this withholding tax. Prospective investors should consult their tax advisors regarding FATCA.

The preceding discussion of U.S. federal tax considerations is for general information only. It is not tax advice. Each prospective investor should consult its own tax advisor regarding the particular U.S. federal, state and local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed change in applicable laws.

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LEGAL MATTERS

Certain legal matters with respect to the securities offered by this prospectus supplement will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Certain legal matters will be passed upon for the underwriters by Ropes & Gray LLP, Boston, Massachusetts.

EXPERTS

The consolidated financial statements of bluebird bio, Inc. appearing in the Company s Annual Report (Form 10-K) for the year ended December 31, 2015, and the effectiveness of bluebird bio, Inc. s internal control over financial reporting as of December 31, 2015 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

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PROSPECTUS

bluebird bio, Inc.

Common Stock

Preferred Stock

Warrants

Units

Debt Securities

By this prospectus, we or any selling stockholder may offer and sell from time to time, in one or more offerings, common stock, preferred stock, warrants, debt securities or any combination thereof as described in this prospectus. The warrants may be convertible into or exercisable or exchangeable for common stock or preferred stock, the preferred stock may be convertible into or exchangeable for common stock and the debt securities may be convertible into or exchangeable for common stock or preferred stock. You should carefully read this prospectus, any prospectus supplement and any free writing prospectus, as well as any documents incorporated in any of the foregoing by reference, before you invest in our securities. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement. The prospectus supplement or any related free writing prospectus may also add to, update, supplement or clarify information contained in this prospectus.

Our common stock is traded on the NASDAQ Global Select Market under the symbol BLUE.

We or any selling stockholder may offer and sell our securities to or through one or more agents, underwriters, dealers or other third parties or directly to one or more purchasers on a continuous or delayed basis. If agents, underwriters or dealers are used to sell our securities, we or any selling stockholder will name them and describe their compensation in a prospectus supplement. The price to the public of our securities and the net proceeds we expect to receive from the sale of such securities will also be set forth in a prospectus supplement. We will not receive any proceeds from the sale of securities by selling stockholders.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISK. YOU SHOULD REVIEW CAREFULLY THE RISKS AND UNCERTAINTIES REFERENCED UNDER THE HEADING RISK FACTORS ON PAGE 6 OF THIS PROSPECTUS AS WELL AS THOSE CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT AND ANY RELATED FREE WRITING PROSPECTUS, AND IN THE OTHER DOCUMENTS THAT ARE INCORPORATED BY REFERENCE INTO THIS PROSPECTUS OR THE APPLICABLE PROSPECTUS SUPPLEMENT.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is July 2, 2014.

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We are responsible for the information contained and incorporated by reference in this prospectus, in any accompanying prospectus supplement, and in any related free writing prospectus we prepare or authorize. We have not authorized anyone to give you any other information, and we take no responsibility for any other information that others may give you. If you are in a jurisdiction where offers to sell, or solicitations of offers to purchase, the securities offered by this documentation are unlawful, or if you are a person to whom it is unlawful to direct these types of activities, then the offer presented in this document does not extend to you. The information contained in this document speaks only as of the date of this document, unless the information specifically indicates that another date applies. Our business, financial condition, results of operations and prospectus may have changed since those dates.

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we filed with the Securities and Exchange Commission, or the SEC, as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration, we and/or selling stockholders may offer shares of our common stock and preferred stock, various series of warrants to purchase common stock or preferred stock, debt securities or any combination thereof, from time to time in one or more offerings. This prospectus only provides you with a general description of the securities we and/or selling stockholders may offer. Each time we and/or selling stockholders offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the specific terms of the offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement. Each such prospectus supplement and any free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents incorporated by reference into this prospectus. We urge you to carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the headings Where You Can Find Additional Information and Incorporation of Certain Information by Reference before you invest in our securities.

Neither we nor any selling stockholder have authorized anyone to provide you with information in addition to or different from that contained in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We take no responsibility for, and can provide no assurances as to the reliability of, any information not contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus that we or a selling stockholder may authorize to be provided to you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate only as of the date on the front of the document and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading Where You Can Find Additional Information.

Unless otherwise mentioned or unless the context requires otherwise, throughout this prospectus, any applicable prospectus supplement and any related free writing prospectus, the words bluebird bio, we, us, our, the company similar references refer to bluebird bio, Inc. and its subsidiaries; and the term securities refers collectively to our common stock, preferred stock, warrants to purchase common stock or preferred stock, debt securities, or any combination of the foregoing securities.

We use Lenti-D and the bluebird bio logo as trademarks in the United States and other countries. We use and have registered LentiGlobin and bluebird bio in the United States. This prospectus and the information incorporated herein by reference contains references to trademarks, service marks and trade names owned by us or other companies. Solely for convenience, trademarks, service marks and trade names referred to in this prospectus and the information incorporated herein, including logos, artwork, and other visual displays, may appear without the ® or symbols, but

such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these

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trademarks, service marks and trade names. We do not intend our use or display of other companies trade names, service marks or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

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WHERE YOU CAN FIND ADDITIONAL INFORMATION

This prospectus is part of a registration statement that we have filed with the SEC. Certain information in the registration statement has been omitted from this prospectus in accordance with the rules of the SEC. We are subject to the information requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC s Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. You may call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room. These documents also may be accessed through the SEC s Electronic Data Gathering, Analysis and Retrieval system, or EDGAR, via electronic means, including the SEC s home page on the Internet (*www.sec.gov*).

We have the authority to designate and issue more than one class or series of stock having various preferences, conversion and other rights, voting powers, restrictions, limitations as to dividends, qualifications, and terms and conditions of redemption. See Description of Securities. We will furnish a full statement of the relative rights and preferences of each class or series of our stock which has been so designated and any restrictions on the ownership or transfer of our stock to any stockholder upon request and without charge. Written requests for such copies should be directed to bluebird bio, Inc., 150 Second Street, Third Floor, Cambridge, Massachusetts 02141, Attention: Secretary, or by telephone request to (339) 499-9300. Our website is located at *http://www.bluebirdbio.com*. Information contained on our website is not incorporated by reference into this prospectus and, therefore, is not part of this prospectus or any accompanying prospectus supplement.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information and reports we file with it, which means that we can disclose important information to you by referring you to these documents. The information incorporated by reference is an important part of this prospectus, and information that we file after the date hereof with the SEC will automatically update and supersede the information already incorporated by reference. We are incorporating by reference the documents listed below, which we have already filed with the SEC, and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, except as to any portion of any future report or document that is not deemed filed under such provisions, after the date of this prospectus and prior to the termination of this offering:

- Annual Report on Form 10-K for the year ended December 31, 2013, as filed with the SEC on March 5, 2014;
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2013 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 24, 2014;
- Quarterly Report on Form 10-Q filed with the SEC for the quarter ended March 31, 2014, as filed with the SEC on May 13, 2014;
- Current Reports on Form 8-K filed with the SEC on January 13, 2014, February 7, 2014, May 22, 2014, June 11, 2014, June 16, 2014 and June 30, 2014 (in each case, except for information contained therein which is furnished rather than filed); and
- The description of our common stock contained in our registration statement on Form 8-A, which was filed with the SEC on June 14, 2013, including any amendment or report filed for the purpose of updating such description.

Upon request, we will provide, without charge, to each person, including any beneficial owner, to whom a copy of this prospectus is delivered a copy of the documents incorporated by reference into this prospectus. You may request a copy of these filings, and any exhibits we have specifically incorporated by reference as an exhibit in this prospectus, at no cost by writing or telephoning us at the following:

bluebird bio, Inc., 150 Second Street, Third Floor, Cambridge, Massachusetts 02141, Attention: Secretary, (339) 499-9300.

You may also access these documents, free of charge on the SEC s website at *www.sec.gov* or on our website at *www.bluebirdbio.com*. The information contained in, or that can be accessed through, our website is not part of this prospectus.

This prospectus is part of a registration statement we filed with the SEC. We have incorporated exhibits into this registration statement. You should read the exhibits carefully for provisions that may be important to you.

Neither we nor any selling stockholder have authorized anyone to provide you with information other than what is incorporated by reference or provided in this prospectus or any prospectus supplement. Neither we nor any selling stockholder are making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus or those documents.

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CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the documents that we incorporate by reference, contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as may, will, could, should, expects, intends, plans, anticipates, believes, estimates, predict continue, and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this report, and in particular those factors referenced in the section Risk Factors.

This prospectus, including the sections entitled About this Prospectus and Risk Factors, contains forward-looking statements that are based on our management s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- 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;
- our ability to advance our viral vector manufacturing and transduction capabilities;
- the timing or likelihood of regulatory filings and approvals;
- the commercialization of our product candidates, if approved;
- the pricing and reimbursement of our product candidates, if approved;
- the implementation of our business model, strategic plans for our business, product candidates and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our product candidates and technology;

estimates of our expenses, future revenues, capital requirements and our needs for additional financing;

the potential benefits of strategic collaboration agreements and our ability to enter into strategic arrangements;

our ability to maintain and establish collaborations or obtain additional grant funding;

our financial performance;

developments relating to our competitors and our industry; and

other risks and uncertainties, including those listed under the caption Risk Factors.

Given these uncertainties, you should not place undue reliance on these forward-looking statements. You should read this prospectus, any supplements to this prospectus and the documents that we incorporate by reference in this prospectus with the understanding that our actual future results may be materially different from what we expect. Except as required by law, we do not undertake any obligation to update or revise any forward-looking statements contained in this prospectus or any supplement to this prospectus, whether as a result of new information, future events or otherwise.

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RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the risks described in the documents incorporated by reference in this prospectus and any prospectus supplement, as well as other information we include or incorporate by reference into this prospectus and any applicable prospectus supplement, before making an investment decision. Our business, financial condition or results of operations could be materially adversely affected by the materialization of any of these risks. The trading price of our securities could decline due to the materialization of any of these risks, and you may lose all or part of your investment. This prospectus and the documents incorporated herein by reference also contain forward-looking statements that involve risks and uncertainties. Actual results could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including the risks described in the documents incorporated herein by reference, including (i) our most recent annual report on Form 10-K which is on file with the SEC and is incorporated herein by reference, (ii) our most recent quarterly report on Form 10-Q, which is on file with the SEC and is incorporated by reference into this prospectus, and (iii) other documents we file with the SEC that are deemed incorporated by reference into this prospectus.

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ABOUT THE COMPANY

We are a clinical-stage biotechnology company focused on transforming the lives of patients with severe genetic and orphan diseases using gene therapy.

We and our scientific collaborators have generated what we believe is human proof-of-concept data for our gene therapy platform in two underserved diseases, each of which has been granted orphan drug status by U.S. and European regulatory authorities. We are conducting a Phase II/III clinical study with our most advanced product candidate, Lenti-D, to evaluate its safety and efficacy in subjects with childhood cerebral adrenoleukodystrophy, or CCALD, a rare, hereditary neurological disorder affecting young boys that is often fatal. In October 2013, we announced that the first subject had been treated in this study. We are also planning to conduct an observational study of subjects with CCALD treated by allogeneic hematopoietic stem-cell transplant referred to as the ALD-103 study.

We also are conducting Phase I/II clinical studies in both the United States and Europe of our next most advanced product candidate, LentiGlobin, to evaluate its safety and efficacy in subjects with ß-thalassemia major and, in the European clinical study, sickle cell disease, or SCD, which are rare, hereditary blood disorders that often lead to severe anemia and shortened lifespans. In December 2013, we announced that the first subject with ß-thalassemia major had been treated in our European study. In March 2014, we announced that the first subject with ß-thalassemia major had been treated in our study in the United States. We presented initial results from the European clinical study of ß-thalassemia major at the European Hematology Association Congress in Milan, Italy in June 2014.

We also have an active investigational new drug application in the United States for a Phase I/II clinical study to evaluate the safety and efficacy of LentiGlobin in subjects with severe SCD. We are planning to treat the first SCD patient with our LentiGlobin product candidate in 2014. Orphan drug status has been granted for LentiGlobin for the treatment of SCD by U.S. regulatory authorities.

In March 2013, we announced a global strategic collaboration with Celgene Corporation to discover, develop and commercialize novel, potentially disease-altering gene therapies in oncology. The collaboration focuses on applying gene therapy technology to genetically modify a patient s own T cells to target and destroy cancer cells. Such modified T cells, called chimeric antigen receptor, or CAR, T cells have been shown to have beneficial effects in human clinical trials for patients with B cell lymphomas. The multi-year research and development collaboration has the potential to lead to the development and commercialization of multiple CAR T cell products.

We were incorporated in Delaware in April 1992 under the name Genetix Pharmaceuticals, Inc., and subsequently changed our name to bluebird bio, Inc. in September 2010. Our mailing address and executive offices are located at 150 Second Street, Third Floor, Cambridge, Massachusetts and our telephone number at that address is (339) 499-9300. We maintain an Internet website at the following address: www.bluebirdbio.com. The information on, or that can be accessed through, our website does not constitute part of this prospectus, and you should not rely on any such information in making the decision whether to purchase our common stock. Our common stock trades on the NASDAQ Global Select Market under the symbol BLUE.

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DESCRIPTION OF SECURITIES

We and/or any selling stockholder may offer shares of our common stock and preferred stock, various series of warrants to purchase common stock or preferred stock, debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt, or any combination thereof from time to time in one or more offerings under this prospectus at prices and on terms to be determined at the time of any offering. This prospectus provides you with a general description of the securities we and/or any selling stockholder may offer. Each time we and/or any selling stockholder offer a type or series of securities under this prospectus, we will provide a prospectus supplement and/or free writing prospectus that will describe the specific amounts, prices and other important terms of the securities.

Common Stock. We and/or any selling stockholder may issue and/or sell, as applicable, shares of our common stock from time to time. Holders of shares of our common stock are entitled to one vote for each share held of record on all matters to be voted on by stockholders and do not have cumulative voting rights. Subject to the preferences that may be applicable to any then outstanding preferred stock, the holders of our outstanding shares of common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any outstanding shares of preferred stock.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors will determine the rights, preferences and privileges of the shares of each wholly unissued series, and any qualifications, limitations or restrictions thereon, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at the holder s option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the rights, preferences and privileges of the preferred stock of such series, as well as any qualifications, limitations or restrictions thereon, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Warrants. We may issue warrants for the purchase of common stock and/or preferred stock in one or more series. We may issue warrants independently or together with common stock and/or preferred stock, and the warrants may be attached to or separate from these securities. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

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Units. We may issue, in one or more series, units consisting of common stock, preferred stock, and/or warrants for the purchase of common stock and/or preferred stock in any combination. We urge you to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreement that contains the terms of the units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

We will evidence each series of units by unit certificates that we will issue. Units may be issued under a unit agreement that we enter into with a unit agent. We will indicate the name and address of the unit agent, if applicable, in the prospectus supplement relating to the particular series of units being offered.

Debt Securities. We may issue debt securities, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the particular series of debt securities being offered, as well as the complete indenture that contains the terms of the debt securities. We will file as exhibits to the registration statement of which this prospectus is a part, the form of indenture and any supplemental agreements that describe the terms of the series of debt securities we are offering before the issuance of the related series of debt securities.

We may evidence each series of debt securities we will issue by an indenture that we enter into with a trustee. We will indicate the name and address of the trustee, if applicable, in the prospectus supplement relating to the particular series of debt securities being offered.

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RATIO OF EARNINGS TO FIXED CHARGES

Our ratio of earnings to fixed charges for recently completed fiscal years and any required interim periods will be specified in a prospectus supplement or in a document that we file with the SEC and incorporate by reference in the future.

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USE OF PROCEEDS

Except as described in any prospectus supplement or in any related free writing prospectus that we may authorize to be provided to you, the net proceeds received by us from our sale of the securities described in this prospectus will be added to our general funds and will be used for our general corporate purposes. From time to time, we may engage in additional public or private financings of a character and amount which we may deem appropriate. Unless otherwise set forth in a prospectus supplement, we will not receive any proceeds from the sale of securities by any selling stockholder.

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SELLING STOCKHOLDERS

Selling stockholders are persons or entities that, directly or indirectly, have acquired or will from time to time acquire from us, our securities. Such selling stockholders may be parties to registration rights agreements with us, or we otherwise may have agreed or will agree to register their securities for resale. The initial purchasers of our securities, as well as their transferees, pledges, donees or successors, all of whom we refer to as selling stockholders, may from time to time offer and sell our securities pursuant to this prospectus and any applicable prospectus supplement.

The applicable prospectus supplement will set forth the name of each of the selling stockholders and the number of securities beneficially owned by such selling stockholder that are covered by such prospectus supplement. The applicable prospectus supplement will also disclose whether any of the selling stockholders has held any position or office with, has been employed by or otherwise has had a material relationship with us during the three years prior to the date of the applicable prospectus supplement.

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PLAN OF DISTRIBUTION

We and/or any selling stockholder may sell our securities from time to time in one or more transactions. We and/or any selling stockholder may sell our securities to or through agents, underwriters, dealers, remarketing firms or other third parties or directly to one or more purchasers or through a combination of any of these methods. In some cases, we and/or any selling stockholder or dealers acting with us and/or any selling stockholder or on behalf of us and/or any selling stockholder may also purchase our securities and reoffer them to the public. We and/or any selling stockholder may also offer and sell, or agree to deliver, our securities pursuant to, or in connection with, any option agreement or other contractual arrangement.

Agents whom we designate may solicit offers to purchase our securities.

We and/or any selling stockholder will name any agent involved in offering or selling our securities, and disclose any commissions that we will pay to the agent, in the applicable prospectus supplement.

Unless we and/or any selling stockholder indicate otherwise in the applicable prospectus supplement, agents will act on a best efforts basis for the period of their appointment.

Agents may be deemed to be underwriters under the Securities Act, of any of our securities that they offer or sell.

We and/or any selling stockholder may use an underwriter or underwriters in the offer or sale of our securities.

If we and/or any selling stockholder use an underwriter or underwriters, we will execute an underwriting agreement with the underwriter or underwriters at the time that we reach an agreement for the sale of our securities.

We and/or any selling stockholder will include the names of the specific managing underwriter or underwriters, as well as the names of any other underwriters, and the terms of the transactions, including the compensation the underwriters and dealers will receive, in the applicable prospectus supplement.

The underwriters will use the applicable prospectus supplement, together with the prospectus, to sell our securities.

We may use a dealer to sell our securities.

If we and/or any selling stockholder use a dealer, we will sell our securities to the dealer, as principal.

The dealer will then sell our securities to the public at varying prices that the dealer will determine at the time it sells our securities.

We and/or any selling stockholder will include the name of the dealer and the terms of the transactions with the dealer in the applicable prospectus supplement.

We and/or any selling stockholder may solicit directly offers to purchase our securities, and we may directly sell our securities to institutional or other investors. We and/or any selling stockholder will describe the terms of direct sales in the applicable prospectus supplement.

We and/or any selling stockholder may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) of the Securities Act.

We and/or any selling stockholder will indemnify agents, underwriters and dealers against certain liabilities, including liabilities under the Securities Act. Agents, underwriters and dealers, or their affiliates, may be customers of, engage in transactions with or perform services for us or our respective affiliates, in the ordinary course of business.

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We and/or any selling stockholder may authorize agents and underwriters to solicit offers by certain institutions to purchase our securities at the public offering price under delayed delivery contracts.

If we and/or any selling stockholder use delayed delivery contracts, we will disclose that we are using them in the prospectus supplement and will tell you when we will demand payment and when delivery of our securities will be made under the delayed delivery contracts.

These delayed delivery contracts will be subject only to the conditions that we describe in the prospectus supplement.

We and/or any selling stockholder will describe in the applicable prospectus supplement the commission that underwriters and agents soliciting purchases of our securities under delayed delivery contracts will be entitled to receive.

Unless otherwise specified in connection with a particular underwritten offering of our securities, the underwriters will not be obligated to purchase offered securities unless specified conditions are satisfied, and if the underwriters do purchase any offered securities, they will purchase all offered securities.

In connection with underwritten offerings of the offered securities and in accordance with applicable law and industry practice, the underwriters in certain circumstances are permitted to engage in certain transactions that stabilize the price of our securities. Such transactions consist of bids or purchases for the purpose of pegging, fixing or maintaining the price of our securities. If the underwriters create a short position in our securities in connection with the offering (*i.e.,* if they sell more securities than are set forth on the cover page of the applicable prospectus supplement), the underwriters may reduce that short position by purchasing our securities in the open market or as otherwise provided in the applicable prospectus supplement. The underwriters may also impose a penalty bid, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. In general, purchases of a security for the purpose of stabilization or to reduce a short position could cause the price of the security to be higher than it might be in the absence of such purchases. The imposition of a penalty bid might also have an effect on the price of our securities to the extent that it were to discourage resales of our securities. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and/or any selling stockholder may effect sales of securities in connection with forward sale, option or other types of agreements with third parties. Any distribution of securities pursuant to any forward sale agreement may be effected from time to time in one or more transactions that may take place through a stock exchange, including block trades or ordinary broker s transactions, or through broker-dealers acting either as principal or agent, or through privately-negotiated transactions, or through an underwritten public offering, or through a combination of any such methods of ale, at market prices prevailing at the time of sale, prices relating to such prevailing market prices or at negotiated or fixed prices.

The specific terms of the lock-up provisions, if any, in respect of any given offering will be described in the applicable prospectus supplement.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8.0% of

the aggregate amount of the securities offered by this prospectus.

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LEGAL MATTERS

The validity of the securities being offered by this prospectus will be passed upon by Goodwin Procter LLP, Boston, Massachusetts.

EXPERTS

The consolidated financial statements of bluebird bio, Inc. as of December 31, 2013 and 2012 and for each of the two years in the period ended December 31, 2013 appearing in the Company s Annual Report (Form 10-K) for the year ended December 31, 2013 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

The consolidated financial statements of bluebird bio, Inc. for the year ended December 31, 2011 incorporated by reference in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2013, have been audited by McGladrey LLP, an independent registered public accounting firm, as stated in their report incorporated by reference herein, and have been so incorporated in reliance upon such report and upon the authority of such firm as experts in accounting and auditing.

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3,289,473 Shares

Common Stock

PROSPECTUS SUPPLEMENT

Goldman, Sachs & Co.

BofA Merrill Lynch

Cowen and Company

Wells Fargo Securities

Wedbush PacGrow

December 6, 2016