bluebird bio, Inc.
Form 424B5
December 11, 2017
Table of Contents

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-216178

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion

Preliminary Prospectus Supplement dated December 11, 2017

PROSPECTUS SUPPLEMENT

(To prospectus dated February 22, 2017)

$600,000,000

Common Stock

We are offering up to $600,000,000 of our common stock in this offering.

Our common stock is quoted on the Nasdaq Global Select Market under the symbol BLUE. On December 8, 2017, the last reported sale price of our common stock was $171.15 per share, as reported on the Nasdaq Global Select Market.

Investing in our common stock involves risks. See Risk Factors beginning on page S-11 of this prospectus supplement and in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017, 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.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions	$	$
Proceeds, before expenses, to bluebird bio, Inc.	$	$

The underwriters have the option to purchase up to approximately $90,000,000 of 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 , 2017.

Goldman Sachs & Co. LLC **BofA Merrill Lynch** **J.P. Morgan** **Cowen**

Prospectus supplement dated December , 2017.

Table of Contents

TABLE OF CONTENTS

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.

Table of Contents

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.

Table of Contents

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.

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 100 F 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, 2016, as filed with the SEC on February 22, 2017;

The information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2016 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed), which was filed with the SEC on April 21, 2017;

Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017, June 30, 2017 and September 30, 2017, as filed with the SEC on May 3, 2017, August 2, 2017 and November 1, 2017, respectively;

Table of Contents

Current Reports on Form 8-K filed with the SEC on February 3, 2017, February 13, 2017, May 2, 2017, May 11, 2017, June 5, 2017 (solely with respect to Item 8.01 and the associated Item 9.01 (Exhibit 99.2)), June 8, 2017, June 23, 2017, June 26, 2017, June 28, 2017, September 20, 2017 (solely with respect to Item 5.02), September 28, 2017, October 4, 2017 (as amended on October 20, 2017), November 1, 2017 (solely with respect to Item 8.01 and the associated Item 9.01 (Exhibit 99.2)), November 16, 2017, November 29, 2017 (solely with respect to Item 8.01), December 7, 2017 and December 11, 2017; 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.

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.

60 Binney Street

Cambridge MA 02142

Phone: (339) 499-9300

investor@bluebirdbio.com

Attn: Investor Relations

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated 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 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, continu estimate, expect, intend, may, should, would, plan, projected or the negative of such words or other sim 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.

Table of Contents

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-11 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 merely address their symptoms. Our clinical programs in severe genetic diseases include our LentiGlobin® product candidate as a treatment for each of transfusion-dependent ß-thalassemia, or TDT, and severe sickle cell disease, or severe SCD, and our Lenti-D product candidate as a treatment for cerebral adrenoleukodystrophy, or CALD, a rare hereditary neurological disorder. Our programs in oncology are built upon our leadership in lentiviral gene delivery and T cell engineering, with a focus on developing novel T cell-based immunotherapies, including chimeric antigen receptor (CAR) and T cell receptor (TCR) T cell therapies. bb2121 and bb21217, our product candidates in oncology, are CAR T cell product candidates for the treatment of multiple myeloma, which we have exclusively licensed to Celgene Corporation, or Celgene.

We are conducting five clinical studies of our LentiGlobin product candidate: a Phase I/II study in the United States, Australia, and Thailand for the treatment of subjects with TDT, called the Northstar Study (HGB-204); a multi-site, international, Phase III study for the treatment of subjects with TDT and a non-$ß^0$/ $ß^0$ genotype, called the Northstar-2 Study (HGB-207); a multi-site, international, Phase III study for the treatment of subjects with TDT and a $ß^0$/$ß^0$ genotype, called the Northstar-3 Study (HGB-212); a single-center Phase I/II study in France for the treatment of subjects with TDT or severe SCD (HGB-205); and a multi-site Phase I study in the United States for the treatment of subjects with severe SCD (HGB-206). We have achieved our enrollment target of 18 patients in the Northstar Study, and we have achieved our enrollment target for the adult and adolescent cohort in the Northstar-2 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 the treatment of both ß-thalassemia and SCD. Our LentiGlobin product candidate was granted Fast-Track designation by the FDA for the treatment of ß-thalassemia major and for the treatment of certain patients with severe SCD. The FDA has granted Breakthrough Therapy designation to our LentiGlobin product candidate for the treatment of transfusion-dependent patients with ß-thalassemia major, and Regenerative Medicine Advanced Therapy designation to our LentiGlobin product candidate for the treatment of severe SCD. The EMA has granted eligibility to its Priority Medicines (PRIME) scheme for our LentiGlobin product candidate for the treatment of TDT. Based on our discussions with the EMA, we believe that we may be able to seek conditional approval for our LentiGlobin product candidate, with our improved manufacturing process, for the treatment of subjects with TDT and a non- $ß^0$/ $ß^0$ genotype on the basis of the totality of the clinical data from our ongoing studies with LentiGlobin. For efficacy, we believe that the Northstar Study and supportive ongoing HGB-205

study, together with the data available from our ongoing Northstar-2 Study and our long-term follow-up study LTF-303, could support the filing of a marketing authorization application in the European Union. This plan is contingent upon all of the studies conducted in patients with TDT with the LentiGlobin product candidate demonstrating sufficient efficacy and safety, and in particular, transfusion independence (the primary endpoint) and reduction in transfusion requirements (a secondary endpoint), for efficacy analyses in the Northstar, HGB-205 and Northstar-2 studies.

We are conducting a multi-site, international, Phase II/III clinical study of our Lenti-D product candidate, called the Starbeam Study (ALD-102), for the treatment of subjects with CALD, a rare, hereditary neurological disorder that is often fatal. Our Lenti-D product candidate has been granted Orphan Drug status by the FDA and the EMA for the treatment of adrenoleukodystrophy. Seventeen subjects were treated with our Lenti-D product candidate in the initial cohort of the Starbeam Study, and we are enrolling up to eight additional subjects in an expansion cohort of the Starbeam study. 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. 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 Biologics License Application, or BLA, and a Marketing Authorization Application, or MAA, submission in the United States and European Union, respectively. However, 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 Our T Cell-based Immunotherapy Program

In March 2013, we entered into a global strategic collaboration with 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 initiated a Phase I clinical study of bb2121, the first anti-BCMA product candidate from our collaboration, and Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb2121. In December 2017, Celgene announced that it began enrollment in a pivotal trial for bb2121 in relapsed/refractory multiple myeloma, and disclosed plans to conduct additional clinical studies of bb2121 in earlier lines of treatment. We may elect to co-develop and co-promote bb2121, and any other product candidates in the United States under this collaboration arrangement. The FDA has granted Breakthrough Therapy designation and the EMA has granted PRIME eligibility to the bb2121 product candidate for relapsed and refractory multiple myeloma. In September 2017, we initiated a Phase I clinical study of bb21217, the second anti-BCMA cell product candidate arising from this collaboration with Celgene, and Celgene exercised its option to obtain an exclusive worldwide license to develop and commercialize bb21217. The FDA has granted Orphan Drug status to both bb2121 and bb21217 product candidates.

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

Table of Contents

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.

Manufacturing Arrangements

In November 2017, we purchased a partially completed manufacturing facility located in Durham, North Carolina for $11.5 million. We acquired this 125,000 square foot facility to provide manufacturing capacity for lentiviral vector in support of our gene and cell therapy product candidates. We have also entered into multi-year agreements with manufacturing partners in the United States and Europe (Brammer Bio, Novasep and MilliporeSigma), which are partnering with us on production of lentiviral vector across all of our programs. In addition, we partner with Lonza Houston, Inc. and apceth Biopharma to produce drug product for Lenti-D and LentiGlobin.

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, 2017, 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.
- 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.

We cannot be certain that the ongoing clinical trial, together with the planned pivotal trial, of the bb2121 product candidate in subjects with relapsed/refractory multiple myeloma will be sufficient to form the basis for a BLA submission for the bb2121 product candidate.

Table of Contents

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-3 clinical study in patients with TDT and 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.

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 60 Binney 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.

Table of Contents

THE OFFERING

Common stock offered by us	shares. We have also granted the underwriters a 30-day option to purchase up to additional shares.
Common stock outstanding following the offering	shares (or shares if the underwriters exercise their option to purchase additional shares in full).
Use of proceeds	We estimate that the net proceeds from this offering will be approximately $569.7 million (or approximately $655.2 million if the underwriters exercise their option to purchase additional shares in full), based on an assumed public offering price of $171.15 per share, the closing price of our common stock on the Nasdaq Global Select Market on December 8, 2017, after deducting estimated underwriting discounts and commissions and estimated offering expenses. We intend to use the net proceeds from this offering 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 Corporation, in the United States following the completion of the ongoing Phase I clinical study; to fund our Phase I clinical study of our bb21217 product candidate in multiple myeloma; to fund HGB-212, our Phase III clinical study of our LentiGlobin product candidate in patients with TDT who have a β^0/β^0 genotype; to further build our commercial infrastructure in support of potential commercial launch of LentiGlobin in TDT in the United States and Europe pending regulatory approvals in the United States and Europe, including the completion of our internal manufacturing capacity; to fund potential future development of our sickle cell program; to fund the continued research and development of additional CAR T and TCR product candidates in oncology; to further expand our manufacturing platform and capabilities to support our ongoing and anticipated product development efforts, and in anticipation of a potential commercial launch; 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-11 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.

Table of Contents

The number of shares of our common stock to be outstanding after the offering is based on 45,785,053 shares of common stock outstanding as of September 30, 2017, and excludes:

- 4,015,728 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2017, at a weighted average exercise price of $63.62 per share;
- 455,672 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2017;
- 1,699,219 shares of common stock reserved for future issuance under our 2013 Stock Option and Incentive Plan, or the 2013 Plan, as of September 30, 2017, 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
- 188,344 shares of common stock reserved for future issuance under our 2013 Employee Stock Purchase Plan as of September 30, 2017.

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

- no exercise by the underwriters of their option to purchase up to approximately $90,000,000 of additional shares of common stock in this offering; and
- no exercise of stock options after September 30, 2017.

Table of Contents

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, 2017, filed with the SEC on November 1, 2017, 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, 2016 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 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 $174.78 on December 8, 2017 and a low price of $60.95 on January 3, 2017 in the twelve-month period ending on December 8, 2017. 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, 2016, our Quarterly Report on Form 10-Q for the quarter ended September 30, 2017 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 may 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, 2017 after subtracting our liabilities. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of $137.07 per share, based on the difference between the assumed public offering price of $171.15 per share, the closing price on the

Nasdaq Global Select Market on December 8, 2017, and the as adjusted pro forma net tangible book value per share of our outstanding common stock as of September 30, 2017.

Table of Contents

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 to our employees. In addition, as of September 30, 2017, options to purchase 4,015,728 shares of our common stock at a weighted average exercise price of $63.62 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, 2017, we had outstanding 45,785,053 shares of our common stock. As of September 30, 2017, we had outstanding options to purchase 4,015,728 shares of our common stock (of which 2,036,608 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 249,872 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. Any actual or perceived weakness in the

economy in general could increase the volatility of the stock market, which may adversely affect the market price of our common stock.

Table of Contents

Tax reform may significantly affect our operations and stockholders.

The Trump Administration and the U.S. Congress are considering substantial revisions to U.S. federal income tax law, and such revisions could significantly impact our company and our operations. There is substantial uncertainty around the likelihood, timing and details of any such tax reform being enacted, but any such reform, if enacted, could have a significant impact on our company and its stockholders. Potential investors should consult their tax advisors about such developments, and their potential impact before investing in our securities.

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the sale of shares of common stock that we are selling in this offering will be approximately $569.7 million based on the assumed sale of 3,505,696 shares of our common stock offered hereby, or approximately $655.2 million if the underwriters exercise in full their option to purchase an assumed 525,854 additional shares of common stock, at an assumed public offering price of $171.15 per share, the closing price of our common stock on the Nasdaq Global Select Market on December 8, 2017, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

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

- 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 Corporation, in the United States following the completion of the ongoing Phase I clinical study;
- To fund our Phase I clinical study of our bb21217 product candidate in multiple myeloma;
- To fund HGB-212, our Phase III clinical study of our LentiGlobin product candidate in patients with TDT who have a $ß^0/ß^0$ genotype;
- To further build our commercial infrastructure in support of potential commercial launch of LentiGlobin in TDT in the United States and Europe pending regulatory approvals in the United States and Europe, including the completion of our internal manufacturing capacity;
- To fund potential future development of our sickle cell program;
- To fund the continued research and development of additional CAR T and TCR product candidates in oncology; and
- To further expand our manufacturing platform and capabilities to support our ongoing and anticipated product development efforts, and in anticipation of a potential commercial launch.

We expect to use any 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 net 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.

Table of Contents

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, 2017, we had net tangible book value of approximately $1.1 billion, or $24.25 per share of our common stock, based upon 45,785,053 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 assumed sale of 3,505,696 shares of common stock in this offering at an assumed public offering price of $171.15 per share (the last reported sale price on the Nasdaq Global Select Market on December 8, 2017), and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2017 would have been approximately $1.7 billion, or approximately $34.08 per share of common stock. This represents an immediate increase in as adjusted net tangible book value of $9.83 per share to our existing stockholders and an immediate dilution of $137.07 per share to investors participating in this offering at the public offering price. The following table illustrates this per share dilution:

Assumed public offering price per share		$ 171.15
Historical net tangible book value per share as of September 30, 2017	$ 24.25	
Increase in net tangible book value per share attributable to new investors	$ 9.83	
As adjusted net tangible book value per share after this offering		$ 34.08
Dilution per share to new investors		$ 137.07

Each $1.00 increase (decrease) in the assumed public offering price of $171.15 per share, the last reported sale price of our common stock on the Nasdaq Global Select Market on December 8, 2017, would (decrease) increase the number of shares of common stock to be issued by us in this offering by (20,363) and 20,604, respectively, assuming the aggregate dollar amount of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same. We may also increase or decrease the aggregate dollar amount of shares we are offering. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

The foregoing table and discussion is based on 45,785,053 shares of common stock outstanding as of September 30, 2017, and excludes:

- 4,015,728 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2017, at a weighted average exercise price of $63.62 per share;

455,672 shares of common stock issuable upon the vesting of restricted stock units outstanding as of September 30, 2017;

1,699,219 shares of common stock reserved for future issuance under the 2013 Plan as of September 30, 2017; and

188,344 shares of common stock reserved for future issuance under our 2013 Employee Stock Purchase Plan as of September 30, 2017.

If the underwriters exercise in full their option to purchase an assumed 525,854 additional shares of common stock at an assumed public offering price of $171.15 per share, the as adjusted net tangible book value

Table of Contents

after this offering would be $35.44 per share, representing an increase in net tangible book value of $11.19 per share to existing stockholders and immediate dilution in net tangible book value of $135.71 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.

Table of Contents

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, 2017, there were 45,785,053 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 legall