PROSPECTUS SUPPLEMENT (To Prospectus dated February 18, 2020)

20,000,000 Shares of Common Stock



We are offering 20,000,000 shares of our common stock at a public offering price of \$6.00 per share.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "BLUE." On January 18, 2023, the last reported sale price of the common stock on the Nasdaq Global Select Market was \$6.03 per share. Investors that purchase shares of our common stock may lose a significant portion of their investments if the price of our common stock declines. Please see the section of this prospectus supplement titled "Risk Factors." You are urged to obtain current market quotations of our common stock.

Investing in the common stock involves risks. See "<u>Risk Factors</u>" beginning on page S-7 and in the related sections noted in the accompanying prospectus, and in the documents incorporated by reference herein and therein. You should carefully read this entire prospectus supplement and the accompanying prospectus, including any information incorporated by reference, before making an investment decision.

	Per Share of Common	
	Stock	Total
Price to the public	\$ 6.00	\$ 120,000,000.00
Underwriting discounts and commissions(1)	\$ 0.30	\$ 6,000,000.00
Proceeds, before expenses, to us	\$ 5.70	\$ 114,000,000.00

(1) See "Underwriting" for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.

We have granted the underwriters an option for a period of up to 30 days from the date of this prospectus supplement to purchase up to 3,000,000 additional shares of our common stock at the public offering price, less the underwriting discounts and commissions. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$6,900,000 and the total proceeds to us, before expenses, will be \$131,100,000.

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

The underwriters expect to deliver the common stock to the investors in book-entry form through the facilities of The Depository Trust Company on or about January 23, 2023.

Goldman Sachs & Co. LLC

J.P. Morgan

The date of this prospectus supplement is January 18, 2023.

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TABLE OF CONTENTS

Prospectus Supplement

	Page
ABOUT THIS PROSPECTUS SUPPLEMENT	S-1
PROSPECTUS SUPPLEMENT SUMMARY	S-3
THE OFFERING	S-5
RISK FACTORS	S-7
CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS	S-11
<u>USE OF PROCEEDS</u>	S-13
DIVIDEND POLICY	S-14
DILUTION	S-15
MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS	S-17
UNDERWRITING	S-21
LEGAL MATTERS	S-29
EXPERTS	S-29
WHERE YOU CAN FIND ADDITIONAL INFORMATION; INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	S-30

Prospectus

	Page
ABOUT THIS PROSPECTUS	1
WHERE YOU CAN FIND ADDITIONAL INFORMATION	2
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	2
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	3
<u>RISK FACTORS</u>	4
ABOUT THE COMPANY	4
DESCRIPTION OF SECURITIES	6
USE OF PROCEEDS	8
SELLING STOCKHOLDERS	8
PLAN OF DISTRIBUTION	9
LEGAL MATTERS	11
<u>EXPERTS</u>	11

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in 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, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. Before you invest, you should carefully read this prospectus supplement, the accompanying prospectus, all information incorporated by reference herein and therein, as well as the additional information described under "Where You Can Find Additional Information; Incorporation by Reference" on page S-30 of this prospectus supplement. These documents contain information you should consider when making your investment decision. This prospectus supplement may add, update or change information contained in the accompanying prospectus. To the extent that any statement that we make in this prospectus supplement is inconsistent with statements made in the accompanying prospectus or any documents incorporated by reference, the statements made in this prospectus supplement will be deemed to modify or supersede those made in the accompanying prospectus and such documents incorporated by reference.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectuses we may provide to you in connection with this offering. Neither we nor any of the underwriters have authorized any other person to provide you with any information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell, and seeking offers to buy, the securities offered hereby only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the securities offered hereby in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement must inform themselves about, and observe any restrictions relating to, the offering of the securities offered hereby and the distribution of this prospectus supplement outside the United States. This prospectus supplement does not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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.

Unless otherwise indicated, information contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference, concerning our industry and the markets in which we operate, including our general expectations and market position, market opportunity and market share, is based on information from our own management estimates and research, as well as from industry and general publications and research, surveys and studies conducted by third parties. Management estimates are derived from publicly available information, our knowledge of our industry and assumptions based on such information and knowledge, which we believe to be reasonable. In addition, assumptions and estimates of our and our industry's future performance are necessarily subject to a high degree of uncertainty and risk due to a variety of factors, including those described in "Risk Factors" in this prospectus supplement, the accompanying prospectus and in our Annual Report on Form 10-K for the year ended December 31, 2021 and Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022, which are incorporated by reference into this prospectus supplement. These and other important factors could cause our future performance to differ materially from our assumptions and estimates. See "Cautionary Note Regarding Forward-Looking Statements."

When we refer to "bluebird," "we," "our," "us" and the "Company" in this prospectus supplement, we mean bluebird bio, Inc. and its consolidated subsidiaries, unless otherwise specified.

This prospectus supplement also includes trademarks, tradenames and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus supplement appear without the $^{\textcircled{m}}$ and $^{\texttt{TM}}$ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information about us, this offering and information appearing elsewhere in this prospectus supplement, in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information you should consider before investing in our securities. Before making an investment decision, to fully understand this offering and its consequences to you, you should carefully read this entire prospectus supplement and the accompanying prospectus, including "Risk Factors" beginning on page S-7 of this prospectus supplement and the financial statements and related notes and the other information that we incorporate by reference into this prospectus supplement.

Company Overview

We are a biotechnology company committed to researching, developing, and commercializing potentially curative gene therapies for severe genetic diseases based on our lentiviral vector gene addition platform. In August 2022, the U.S. Food and Drug Administration (the "FDA") approved ZYNTEGLO (betibeglogene autotemcel, also known as beti-cel), for the treatment of adult and pediatric patients with β-thalassemia who require regular red blood cell transfusions. In September 2022, the FDA granted Accelerated Approval of SKYSONA (elivaldogene autotemcel, also known as eli-cel), to slow the progression of neurologic dysfunction in boys 4-17 years of age with early active cerebral adrenoleukodystrophy ("CALD") and, also in September 2022, prior to the completion of its review of the SKYSONA Biologics License Application ("BLA"), the FDA lifted the previous clinical hold on SKYSONA that was put in place in August 2021. We have agreed to provide confirmatory long-term clinical data to the FDA as a condition of the SKYSONA Accelerated Approval, and continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. ZYNTEGLO is available exclusively through Qualified Treatment Centers ("QTCs"). Apheresis (cell collection) has occurred for the first patients to be treated commercially with ZYNTEGLO and SKYSONA.

We received Rare Pediatric Disease Priority Review Vouchers ("PRVs") upon the FDA's approval of both ZYNTEGLO and SKYSONA and, in the fourth quarter of 2022, we completed the sale of the PRV that we received in connection with the accelerated approval of SKYSONA for \$102 million in gross proceeds. Additionally, on January 5, 2023, we completed the sale of the PRV that we received in connection with the approval of ZYNTEGLO for \$95 million in gross proceeds.

We are also developing lovotibeglogene autotemcel, also known as lovo-cel, as a treatment for patients with sickle cell disease ("SCD"). Based on our discussions with the FDA, we plan to seek approval for lovo-cel for patients 12 and older in the United States on the basis of clinical data for efficacy from HGB-206 Group C, with supporting data from HGB-210. We have treated all of the patients who will form the primary basis of efficacy for approval. In December 2022, we completed analytical comparability studies, as the key remaining action prior to our planned BLA submission in the first quarter of 2023. In December 2022, the FDA lifted a partial clinical hold on our clinical program for lovo-cel for patients under the age of 18, which had been in place since December 2021.

We estimate that there are approximately 22,000 patients with ß-thalassemia, CALD and SCD in the United States who are potentially addressable by ZYNTEGLO, SKYSONA and, if approved, lovo-cel, with 20,000 of these patients estimated to have SCD, 1,300-1,5000 estimated to have ß-thalassemia and 40 estimated to have CALD. However, the industry in which we operate is subject to a high degree of uncertainty and risk, and these estimates could change.

Financial Update

As of December 31, 2022, our cash, cash equivalents and marketable securities were approximately \$182 million, excluding restricted cash of approximately \$45 million, which was not released in the fourth quarter of 2022.

The cash, cash equivalents and marketable securities information above is based on preliminary unaudited information and management estimates for the year ended December 31, 2022, is not a comprehensive statement of our financial results as of and for the fiscal year ended December 31, 2022, and is subject to completion of our financial closing procedures. Our independent registered public accounting firm has not conducted an audit or review of, and does not express an opinion or any other form of assurance with respect to, this preliminary estimate.

We expect our existing cash, cash equivalents, restricted cash and marketable securities, including the proceeds from the sale of the ZYNTEGLO PRV, will be sufficient to meet our planned operating expenses and capital expenditure requirements into the first quarter of 2024. We have based this estimate on assumptions that may prove to be incorrect, including our ability to access our restricted cash, and we could expend our available capital resources at a rate greater than we currently expect.

Corporate 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 455 Grand Union Boulevard, Somerville, 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.

	THE OFFERING
Common stock offered by us	20,000,000 shares at a public offering price of \$6.00 per share.
Common stock to be outstanding immediately after thi offering	s 102,923,298 shares (or 105,923,298 shares if the underwriters exercise in full their option to purchase additional shares).
Option to purchase additional Shares of common stock	The underwriters have a 30-day option to purchase up to 3,000,000 additional shares of our common stock at the public offering price less underwriting discounts and commissions.
Use of proceeds	We estimate the net proceeds from this offering will be approximately \$113.55 million after deducting underwriting discounts and commissions and estimated offering expenses payable by us.
	We currently intend to use the net proceeds from this offering, together with our existing cash:
	• to support commercialization and manufacturing for its two approved gene therapies, ZYNTEGLO and SKYSONA;
	• to accelerate future commercialization activities for its gene therapy candidate, lovo- cel, for sickle cell disease, if approved; and
	• to fund working capital and other general corporate purposes.
	See "Use of Proceeds" on page S-13 for more information.
Risk factors	Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-7 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement for a discussion of factors that you should read and consider before investing in our securities.
Listing	Our common stock is listed on the Nasdaq Global Select Market under the symbol "BLUE."
Transfer agent	American Stock Transfer & Trust Company, LLC
The number of shares of common stock to be out outstanding as of December 31, 2022, and excludes:	standing immediately after this offering is based on 82,923,298 shares of common stock

- 4,440,142 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2022, at a weighted average exercise price of \$35.00 per share;
- 2,521,473 shares of common stock issuable upon the vesting of restricted stock units ("RSUs") outstanding as of December 31, 2022;
- 2,272,727 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2022;

- 5,753,820 shares of common stock reserved for future issuance under our 2013 Stock Option and Incentive Plan ("the 2013 Plan") as of December 31, 2022, 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;
- 1,279,312 shares of common stock reserved for future issuance under our 2013 Employee Stock Purchase Plan ("ESPP") as of December 31, 2022; and
- 828,383 shares of common stock reserved for future issuance under our 2021 Inducement Plan ("Inducement Plan") as of December 31, 2022.

Unless otherwise indicated, all information contained in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares of our common stock and no exercise of the outstanding options and RSUs described above.



RISK FACTORS

Investing in our securities involves a high degree of risk. Before investing in our securities, you should consider carefully the risks described below, together with the other information contained in this prospectus supplement, the accompanying prospectus or incorporated by reference herein or therein, including the risks and uncertainties discussed under "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2021 and Quarterly Reports on Form 10-Q for the quarters ended March 31, 2022, June 30, 2022 and September 30, 2022, which are incorporated by reference into this prospectus supplement. If any of the risks incorporated by reference or set forth below occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our securities could decline, and you may lose all or part of your investment.

Risks Related to this Offering

Purchasers of our securities in this offering will experience immediate and substantial dilution in the book value of their investment. You may experience further dilution upon exercise of options and warrants and settlement of RSUs.

The public offering price per share of common stock in this offering is substantially higher than the net tangible book value per share of our common stock before giving effect to this offering. Accordingly, if you purchase securities in this offering, you will incur immediate substantial dilution of \$3.41 per share, representing the difference between the public offering price per share of common stock and our as adjusted net tangible book value as of September 30, 2022. Furthermore, if outstanding options or warrants are exercised or outstanding RSUs are settled, you could experience further dilution. For a further description of the dilution that you will experience immediately after this offering, see the section in this prospectus supplement entitled "Dilution."

We have broad discretion to determine how to use the funds raised in this offering, and may use them in ways that may not enhance our operating results or the price of our common stock.

Our management will have broad discretion over the use of proceeds from this offering, and we could spend the proceeds from this offering in ways our stockholders may not agree with or that do not yield a favorable return, if at all. We intend to use the net proceeds to support commercialization and manufacturing for its two approved gene therapies, ZYNTEGLO and SKYSONA, to accelerate future commercialization activities for its gene therapy candidate, lovo-cel, for sickle cell disease, if approved, and to fund working capital and other general corporate purposes. However, our use of these proceeds may differ substantially from our current plans. If we do not invest or apply the proceeds of this offering in ways that improve our operating results, we may fail to achieve expected financial results, which could cause our stock price to decline.

There is substantial doubt regarding our ability to continue as a going concern. We will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently advancing our programs in severe genetic diseases through preclinical and clinical development. Developing and commercializing gene therapy products is expensive, and we cannot determine with certainty when or to what extent we will generate meaningful product revenues from the commercialization and sale of our approved products and planned commercial launches.

As of September 30, 2022, we had cash and cash equivalents, and marketable securities of approximately \$141.0 million. As of December 31, 2021, our cash, cash equivalents and marketable securities were \$396.6 million. Based on our current business plan as of the date of our unaudited condensed consolidated

financial statements appearing in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2022, we expect that our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, when filed with the Securities and Exchange Commission, and the report of our auditors contained therein, whether or not this offering is successful, will reflect there is substantial doubt regarding our ability to continue as a going concern for a period of one year after such date.

In April 2022, we announced a comprehensive restructuring plan intended to reduce operating expenses. We may not realize expected cost savings from the implementation of these plans at the levels we expect; we may encounter additional delays in the development of our programs, including the imposition of new clinical holds, that may impact our ability to meet our expected time lines and increase our costs; the internal and external costs required for our ongoing and planned activities, and the resulting impact on expense and use of cash, may be higher than expected which may cause us to use cash more quickly than we expect or change or curtail some of our plans or both; we expect our operating expenses to increase significantly as we continue commercialization activities for ZYNTEGLO and SKYSONA and prepare for commercialization of lovo-cel, if approved; our expectations as to expenses, cash usage and cash needs may prove not to be correct for other reasons such as changes in plans or actual events being different than our assumptions. We will need to raise additional funding in order to execute on our current business plans and strategy.

Our efforts to raise additional funding or reduce expenses may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our approved products. In addition, we cannot guarantee that financing will be available in sufficient amounts or on terms acceptable to us, if at all. Moreover, the terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would dilute all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and we may be required to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than otherwise would be desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, or if revenues from collaboration arrangements or product sales are less than we have projected, we may be required to further revise our business plan and strategy, which may result in us significantly curtailing, delaying or discontinuing one or more of our research or development programs or the commercialization of any product candidates or may result in our being unable to expand our operations or otherwise capitalize on our business opportunities. As a result, our business, financial condition and results of operations could be materially affected.

If the distribution of shares of 2seventy bio, together with certain related transactions, does not qualify as a transaction that is generally tax-free for U.S. federal income tax purposes, we and our stockholders could be subject to significant tax liabilities.

The completion of the distribution of shares of 2seventy bio was conditioned upon, among other things, our receipt of a private letter ruling from the U.S. Internal Revenue Service, or the IRS, and an opinion from Goodwin Procter LLP, both satisfactory to our board of directors and both continuing to be valid, together confirming that the distribution, together with certain related transactions, generally is tax-free for U.S. federal income tax purposes under Sections 355 and 368(a)(1)(D) of the U.S. Internal Revenue Code of 1986, as amended, or the Code. We have received a favorable private letter ruling from the IRS addressing one significant issue of the qualification of the distribution under Section 355 of the Code. However, the private letter ruling does not address the remaining issues that are relevant to determining whether the distribution, together with certain related transactions, qualifies as a transaction that is generally tax-free for U.S. federal income tax

purposes. This can include events that occur following the distribution such as subsequent public offerings by us or 2seventy bio or shares sales to persons that engaged in negotiations over share purchases prior to the distribution. Subsequent tax opinions have been obtained by us and 2seventy bio in connection with certain post-distribution sales of 2seventy bio's shares. The IRS private letter ruling and opinion of Goodwin Procter LLP and tax opinions relating to certain subsequent post-distribution sales of 2seventy bio shares were based, among other things, on various facts and assumptions, as well as certain representations, statements and undertakings from us and 2seventy bio (including those relating to the past and future conduct of us and 2seventy bio) and were subject to certain caveats. If any of these facts, assumptions, representations, statements or undertakings is, or becomes, inaccurate or incomplete, or if we or 2seventy bio breach any of our respective covenants relating to the separation, the IRS private letter ruling and tax opinion may be invalid. Moreover, the opinion is not binding on the IRS or any courts. Accordingly, notwithstanding receipt of the IRS private letter ruling and an opinion of Goodwin Procter LLP at the time of the distribution, the IRS could determine that the distribution and certain related transactions should be treated as taxable transactions for U.S. federal income tax purposes. If the distribution, together with certain related transactions, were to fail to qualify as a transaction that is generally tax-free under Sections 355 and 368(a)(1)(D) of the Code, in general, for U.S. federal income tax purposes, we would recognize taxable gain as if we have sold 2seventy bio's distributed common stock in a taxable sale for its fair market value and our stockholders who receive shares of 2seventy bio common stock in the distribution would be subject to tax as if they had received a taxable distribution equal to the fair market value of such shares. In connection with the distribution, we and 2seventy bio entered into a tax matters agreement pursuant to which each party is responsible for certain liabilities and obligations following the distribution. In general, under the terms of the tax matters agreement, if the distribution, together with certain related transactions, were to fail to qualify as a transaction that is generally tax-free for U.S. federal income tax purposes under Sections 355 and 368(a)(1)(D) of the Code, and if and to the extent that such failure results from a prohibited change of control in us under Section 355(e) of the Code, or an acquisition of our stock or assets or certain actions, omissions or failures to act, by us, then we will bear any resulting taxes, interest, penalties and other costs. If and to the extent that such failure results from a prohibited change of control in 2seventy bio under Section 355(e) of the Code or an acquisition of 2seventy bio stock or assets or certain actions by 2seventy bio, then 2seventy bio will be obligated to indemnify us for any resulting taxes, interest, penalties and other costs, including any reductions in our net operating loss carryforwards or other tax assets. If such failure does not result from a prohibited change of control in bluebird bio or 2seventy bio under Section 355(e) of the Code and both we and 2seventy bio are responsible for such failure, liability will be shared according to relative fault. If neither we nor 2seventy bio is responsible for such failure, we will bear any resulting taxes, interest, penalties and other costs.

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. Concerns over global stability, including as a result of the COVID-19 pandemic, as well as political and economic conditions in the United States and abroad, have contributed to the extreme volatility of the markets, which may have an effect on the market price of our common stock.

A substantial number of shares of common stock may be sold in the market following this offering, which may depress the market price for our common stock.

Sales of a substantial number of shares of our common stock in the public market, or the perception that such sales could occur, following this offering could cause the market price of our common stock to decline. A substantial majority of the outstanding shares of our common stock are, and the shares of common stock sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act of 1933, as amended. We cannot predict the effect that future sales of shares of our common stock would have on the market price of our common stock.

Insertional oncogenesis is a risk of gene therapies using viral vectors that can integrate into the genome, and several patients with CALD treated with SKYSONA in our clinical studies have been diagnosed with myelodysplastic syndrome ("MDS") likely mediated by Lenti-D LVV insertion. These events may require us to halt or delay further clinical development of our product candidates or to suspend or cease commercialization following marketing approval, and the commercial potential of our products and product candidates may be materially and negatively impacted.

A potentially significant risk in any gene therapy product using viral vectors that can integrate into the genome is that the vector will insert in or near cancer-causing genes, leading to the proliferation of certain cellular clones that can cause cancer in the patient, known as insertional oncogenesis. Several patients with CALD treated with SKYSONA in our clinical studies have been diagnosed with MDS likely mediated by Lenti-D LVV insertion. In addition, we cannot make assurances that additional patients treated with SKYSONA, ZYNTEGLO or lovo-cel in the clinical or commercial setting will not be diagnosed with MDS, leukemia or lymphoma. Patients treated with our therapies, including lovo-cel, have exhibited persistent oligoclonality, in which a portion of their hematopoietic system is comprised of cells containing at least one insertion site, as measured by integration site analysis. Based on our pharmacovigilance protocols, we increase our monitoring of patients who exhibit persistent oligoclonality. It is not clear at this time whether persistent oligoclonality represents an increased risk of developing MDS, leukemia, or lymphoma in the future, but it is a criteria used by the FDA to evaluate the safety of gene therapies over time. There is also the potential risk of other delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material. The FDA has stated that LVV possess characteristics that may pose high risks of delayed adverse events. If any such adverse events occur, further advancement of our clinical studies could be halted or delayed, we may not receive marketing approval for our product candidates, and we may be unable to commercialize our approved products. It is possible that upon occurrence or recurrence of any of these events, the FDA may place one or more of our programs on hold, impose requirements that result in delays for regulatory approval for one or more of our programs, require risk evaluation or mitigation strategies as a condition for regulatory approval, or may cause us to cease commercialization following the receipt of any marketing approval. If any of these were to occur, the commercial potential of our programs may be materially and negatively impacted.

Furthermore, treatment with our products and product candidates involve chemotherapy or myeloablative treatments which can cause side effects or adverse events that may impact the perception of the potential benefits of our products and product candidates. For instance, MDS leading to acute myeloid leukemia is a known risk of certain myeloablative regimens. Additionally, ZYNTEGLO, SKYSONA, or lovo-cel, the procedures associated with their administration, or with the collection of patients' cells, could potentially cause other adverse events that have not yet been predicted. The inclusion of patients with significant underlying medical problems in our clinical studies may result in deaths, or other adverse medical events, due to other therapies or medications that such patients may be using, or the progression of their disease. For instance, it is possible that the events of MDS and acute myeloid leukemia previously reported in our HGB-206 clinical study were caused by lovo-cel, in combination with underlying SCD, transplant procedure, and stress on the bone marrow following drug product infusion. In December 2022, the FDA lifted its partial clinical hold for patients under the age of 18 in studies evaluating lovo-cel for SCD. Notwithstanding the lifting of this partial clinical hold, additional adverse events or new data or analyses regarding previously reported events may indicate significant safety issues, and the FDA could potentially impose or reimpose a clinical hold in the future on studies evaluating lovo-cel. We maintain dialogue with the FDA and, from time to time, as required or requested by the FDA, update the FDA on additional adverse events or new data or analyses regarding previously reported events or new data or analyses regarding previously reported events or new data or analyses regarding previously reported events or new data or analyses regarding previously reported events or new data or analyses regarding previously reported events or new data or analyses regarding previously reported event

Even if a product such as lovo-cel is ultimately approved and although ZYNTEGLO and SKYSONA were approved by the FDA, serious safety events may result in the product being removed from the market or its market opportunity being significantly reduced. Other patients receiving our products and product candidates may develop leukemia, lymphoma, or MDS in the future, which may negatively impact the commercial prospects of our products and product candidates. Any of these events could impair our ability to develop or commercialize our products and product candidates, and their commercial potential may be materially and negatively impacted.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference contain forward-looking statements that involve risks and uncertainties, as well as assumptions that, if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference therein are forward-looking statements. In some cases, you can identify forward-looking statements by words such as "anticipate," "believe," "contemplate," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "seek," "should," "target," "would," or the negative of these words or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the initiation, timing, progress and results of our clinical studies, and our research and development programs;
- our ability to successfully complete clinical studies;
- our ability to obtain adequate financing to fund our operations and to execute on our strategy;
- our ability to establish and scale commercial viral vector and drug product manufacturing capabilities, and to ensure adequate supply of our viral vectors and drug products;
- · the timing or likelihood of regulatory filings and marketing approvals for our product candidates;
- the timing or success of commercialization of any approved products;
- our ability to obtain adequate pricing and reimbursement of any approved products;
- 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, cost savings, cash burn, future revenues, capital requirements and our needs for additional financing;
- our ability to maintain and establish collaborations and licenses;
- developments relating to our competitors and our industry;
- the impact of the COVID-19 pandemic;
- the effects, costs, and benefits of the separation of our portfolio of products and programs into two independent, publicly-traded companies;
- our ability to continue as a going concern;
- estimates of our addressable patient population;
- our expected future revenues, cash runway and planned operating expenses and capital expenditure requirements; and
- our intended use of proceeds from this offering.

Any forward-looking statements in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference reflect our views as of the date on which they are made with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those

listed under "Risk Factors" beginning on page S-7 of this prospectus supplement, in "Item 1A. Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, in "Item 1A. Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2022 and elsewhere in this prospectus supplement, the accompanying prospectus and documents incorporated by reference. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

You should read this prospectus supplement, the accompanying prospectus and the documents that we reference in this prospectus supplement and have filed with the SEC as exhibits to the registration statement of which this prospectus supplement is a part and documents incorporated by reference herein with the understanding that our actual future results, levels of activity, performance and events and circumstances may be materially different from what we expect.

USE OF PROCEEDS

We estimate that the net proceeds from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$113.55 million (or approximately \$130.65 million if the underwriters exercise in full their option to purchase additional shares of our common stock).

We currently intend to use the net proceeds we receive from this offering, together with our existing cash:

- to support commercialization and manufacturing for its two approved gene therapies, ZYNTEGLO and SKYSONA;
- to accelerate future commercialization activities for its gene therapy candidate, lovo-cel, for sickle cell disease, if approved; and
- to fund 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 businesses, technologies, products or assets.

The amount and timing of our actual expenditures will depend upon numerous factors, including the factors described under "Risk Factors" in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, as well as the timing and success of our ongoing clinical studies and the timing of regulatory submissions and potential approvals. 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.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

DILUTION

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

Our historical net tangible book value as of September 30, 2022 was approximately \$153.2 million, or approximately \$1.85 per share. Our historical net tangible book value is the amount of our total tangible assets less our total liabilities. Historical net tangible book value per share represents historical net tangible book value divided by the 82,880,703 shares of common stock outstanding as of September 30, 2022.

After giving effect to the sale of 20,000,000 shares of our common stock in this offering, 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, 2022 would have been approximately \$266.8 million, or approximately \$2.59 per share. This represents an immediate increase in net tangible book value of \$0.74 per share to existing stockholders and immediate dilution in net tangible book value of \$3.41 per share to investors purchasing shares of our common stock in this offering. Dilution per share to new investors is determined by subtracting as adjusted net tangible book value per share after this offering from the public offering price per share of common stock paid by new investors.

The following table illustrates this dilution on a per-share basis:

Public offering price per share		\$6.00
Historical net tangible book value per share as of September 30, 2022	\$1.85	
Increase in as adjusted net tangible book value per share attributable to this offering	0.74	
As adjusted net tangible book value per share after this offering		2.59
Dilution per share to new investors purchasing common stock in this offering		\$3.41

If the underwriters exercise their option to purchase up to 3,000,000 additional shares in full, the pro forma as adjusted net tangible book value will increase to \$2.68 per share, representing an immediate increase in pro forma as adjusted net tangible book value of \$0.83 per share of our common stock to existing stockholders and an immediate dilution of \$3.32 per share to purchasers of our common stock in this offering.

The above table is based on 82,880,703 shares of common stock outstanding as of September 30, 2022, and excludes as of that date:

- 4,547,525 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2022, at a weighted average exercise price of \$36.59 per share;
- 2,472,591 shares of common stock issuable upon the vesting of RSUs outstanding as of September 30, 2022;
- 2,272,727 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2022;
- 5,737,914 shares of common stock reserved for future issuance under the 2013 Plan as of September 30, 2022;
- 1,279,312 shares of common stock reserved for future issuance under our ESPP as of September 30, 2022; and
- 828,383 shares of common stock reserved for future issuance under our Inducement Plan as of September 30, 2022.

To the extent that any options are exercised or RSUs are settled, 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.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or the IRS, in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income and the alternative minimum tax. In addition, it does not address consequences relevant to Non-U.S. Holder's subject to special rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies and other financial institutions;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies" and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation;
- tax-qualified retirement plans; and
- "qualified foreign pension funds" as defined in Section 897(1)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR

SITUATIONS 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 LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a "Non-U.S. Holder" is any beneficial owner of our common stock that is neither a "U.S. person" nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and all substantial decisions of which are subject to the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section titled "Dividend Policy," we have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "—Sale or Other Taxable Disposition."

Subject to the discussion below regarding effectively connected income, dividends paid to a Non-U.S. Holder will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable tax treaties.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States. Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Sale or Other Taxable Disposition

A Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

- the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);
- the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest, or USRPI, by reason of our status as a U.S. real property holding corporation, or USRPHC, for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular rates applicable to U.S. persons. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

A Non-U.S. Holder described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on gain realized upon the sale or other taxable disposition of our common stock, which may be offset by certain U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition of our common stock by a Non-U.S. Holder will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market and such Non-U.S. Holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the Non-U.S. Holder certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any distributions on our common stock paid to the Non-U.S. Holder, regardless of whether such distributions constitute dividends or whether any tax was actually withheld.

In addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.related brokers generally will not be subject to backup withholding or information reporting if the applicable withholding agent receives the certification described above or the Non-U.S. Holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker that does not have certain enumerated relationships with the United States generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withhold under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or FATCA) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or (subject to the proposed Treasury Regulations discussed below) gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations and administrative guidance, withholding under FATCA generally applies to payments of dividends on our common stock. While withholding under FATCA would have applied also to payments of gross proceeds from the sale or other disposition of stock on or after January 1, 2019, proposed Treasury Regulations eliminate FATCA withholding on payments of gross proceeds entirely. Taxpayers generally may rely on these proposed Treasury Regulations until final Treasury Regulations are issued.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

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. LLC and J.P. Morgan Securities LLC are the representatives of the underwriters.

<u>Underwriters</u>	Number of Shares of Common Stock
Goldman Sachs & Co. LLC	11,000,000
J.P. Morgan Securities LLC	9,000,000
Total	20,000,000

The underwriters are committed to take and pay for all of the shares of common stock 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 3,000,000 additional shares of common stock from us. They may exercise that option for 30 days. If any shares of common stock are purchased pursuant to this option, the underwriters will severally purchase shares of common stock in approximately the same proportion as set forth in the table above.

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 3,000,000 additional shares.

Paid by the Company	No Exercise		Full Exercise	
Per Share of Common Stock	\$ 0.30	\$	0.30	
Total	\$ 6,000,000.00	\$ 6	5,900,000.00	

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 supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount of up to \$0.18 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 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 (subject to a certain limited exception), 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 to be sold by us in this offering;
- the issuance by us of shares of common stock upon the exercise of an option, the settlement of a restricted stock unit, or warrant or share of preferred stock;
- 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;
- the entry by us into an at-the-market equity offering program with Goldman Sachs & Co. LLC, as sales agent, and the filing by us of a preliminary prospectus supplement with respect to shares of common stock to be issued and sold under such program; 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 for which 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 supplement to third parties in privately negotiated transactions. In connection with those derivatives, the third parties may sell securities covered by this prospectus supplement, 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 \$450,000.

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 (each, a "Relevant Member State"), no shares of common stock have been offered or will be offered pursuant to the offering to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares of common stock which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in

another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Regulation, except that offers of the shares of common stock may be made to the public in that Relevant Member State at any time under the following exemptions under the Prospectus Regulation:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Regulation;
- (b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Regulation), subject to obtaining the prior consent of the representatives; or
- (c) in any other circumstances falling within Article 1(4) of the Prospectus Regulation,

provided that no such offer of shares of common stock shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation. For the purposes of this provision, the expression an 'offer to the public' in relation to the shares of common stock 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 any shares of common stock to be offered so as to enable an investor to decide to purchase any shares of common stock, and the expression "Prospectus Regulation" means Regulation (EU) 2017/1129.

Each person in a Relevant Member State who receives any communication in respect of, or who initially acquires any shares of common stock or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and affiliates and us that:

- (i) it is a "qualified investor" as defined in the Prospectus Regulation; and
- (ii) in the case of any shares of common stock acquired by it as a financial intermediary, as that term is used in Article 5 of the Prospectus Regulation, (a) the shares of common stock acquired by it in the offering have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Relevant Member State other than qualified investors, as that term is defined in the Prospectus Regulation, or have been acquired in other circumstances falling within the points (a) to (d) of Article 1(4) of the Prospectus Regulation and the prior consent of the representatives has been given to the offer or resale; or (ii) where the shares of common stock have been acquired by it on behalf of persons in any Relevant Member State other than qualified investors, the offer of those shares of common stock to it is not treated under the Prospectus Regulation as having been made to such persons.

The company, the underwriters and their affiliates, and others will rely upon the truth and accuracy of the foregoing representation, acknowledgment and agreement. Notwithstanding the above, a person who is not a qualified investor and who has notified the representatives of such fact in writing may, with the prior consent of the representatives, be permitted to acquire shares of common stock in the offering.

United Kingdom

This prospectus supplement and any other material in relation to the shares of common stock described herein is only being distributed to, and is only directed at, and any investment or investment activity to which this prospectus supplement relates is available only to, and will be engaged in only with persons who are (i) persons having professional experience in matters relating to investments who fall within the definition of investment professionals in Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotions) Order 2005 ("FPO"); or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the FPO; (iii) outside the UK; or (iv) persons to whom an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) in connection with the issue or sale of any shares of common stock may otherwise lawfully be communicated or caused to be communicated, (all such persons together being referred to as Relevant Persons). The shares of common stock are only available in the UK to, and any invitation, offer or

agreement to purchase or otherwise acquire the shares of common stock will be engaged in only with, the Relevant Persons. This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other person in the UK. Any person in the UK that is not a Relevant Person should not act or rely on this prospectus or any of its contents.

No shares of common stock have been offered or will be offered pursuant to the offering to the public in the United Kingdom prior to the publication of a prospectus in relation to the shares of common stock which has been approved by the Financial Conduct Authority, except that the shares of common stock may be offered to the public in the United Kingdom at any time:

- (i) to any legal entity which is a qualified investor as defined under Article 2 of the UK Prospectus Regulation;
- to fewer than 150 natural or legal persons (other than qualified investors as defined under Article 2 of the UK Prospectus Regulation), subject to obtaining the prior consent of the Global Coordinators for any such offer; or
- (iii) in any other circumstances falling within Section 86 of the FSMA.
- (iv) provided that no such offer of the shares of common stock shall require the Company and/or any underwriters or any of their affiliates to publish a prospectus pursuant to Section 85 of the FSMA or supplement a prospectus pursuant to Article 23 of the UK Prospectus Regulation. For the purposes of this provision, the expression an "offer to the public" in relation to the shares of common stock in the United Kingdom means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of common stock to be offered so as to enable an investor to decide to purchase or subscribe for any shares of common stock and the expression "UK Prospectus Regulation" means Regulation (EU) 2017/1129 as it forms part of domestic law by virtue of the European Union (Withdrawal) Act 2018.
- (v) Each person in the UK who acquires any shares of common stock in the offering or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with the company, the underwriters and their affiliates that it meets the criteria outlined in this section.

Canada

The shares 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 shares must be made in accordance with an exemption from, 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 prospectus supplement (including any amendment thereto) contains a 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 of common stock 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), or 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), or 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 of common stock 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 of common stock 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 supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares of common stock may not be circulated or distributed, nor may the shares of common stock 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 of common stock 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 of common stock under Section 275 of the SFA except: (i) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (ii) where such transfer arises from an offer in that corporation of law, (v) as specified in Section 276(7) of the SFA, or (vi) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore, or Regulation 32.

Where the shares of common stock 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 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 of common stock under Section 275 of the SFA except: (i) to an institutional investor under Section 274 of the SFA or to a relevant person (as defined in Section 275(2) of the SFA), (ii) 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), (iii) where no consideration is or will be given for the transfer, (iv) where the transfer is by operation of law, (v) as specified in Section 276(7) of the SFA, or (vi) as specified in Regulation 32.

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of shares of common stock, the Company has

determined, and hereby notifies all relevant persons (as defined in Section 309A(1) of the SFA), that the shares are "prescribed capital markets products" (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Japan

The shares 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 shares 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 of common stock 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 of common stock 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 of common stock 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 of common stock 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 of common stock to which this prospectus supplement relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares of common stock offered should conduct their own due diligence on the shares of common stock. If you do not understand the contents of this prospectus supplement you should consult an authorized financial advisor.

Israel

In the State of Israel this prospectus supplement shall not be regarded as an offer to the public to purchase shares of common stock under the Israeli Securities Law, 5728-1968, which requires a prospectus to be published and authorized by the Israel Securities Authority, if it complies with certain provisions of Section 15 of the Israeli Securities Law, 5728-1968, including, inter alia, if: (i) the offer is made, distributed or directed to not more than 35 investors, subject to certain conditions (the "Addressed Investors"); or (ii) the offer is made, distributed or directed to certain qualified investors defined in the First Addendum of the Israeli Securities Law, 5728-1968, subject to certain conditions (the "Qualified Investors"). The Qualified Investors shall not be taken

into account in the count of the Addressed Investors and may be offered to purchase securities in addition to the 35 Addressed Investors. The Company has not and will not take any action that would require it to publish a prospectus in accordance with and subject to the Israeli Securities Law, 5728-1968. The Company and the underwriters have not and will not distribute this prospectus supplement or make, distribute or direct an offer to subscribe for our common stock to any person within the State of Israel, other than to Qualified Investors and up to 35 Addressed Investors.

Qualified Investors may have to submit written evidence that they meet the definitions set out in of the First Addendum to the Israeli Securities Law, 5728-1968. In particular, we may request, as a condition to be offered common stock, that Qualified Investors will each represent, warrant and certify to us and/or to anyone acting on our behalf: (i) that it is an investor falling within one of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968; (ii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968; (iii) which of the categories listed in the First Addendum to the Israeli Securities Law, 5728-1968 regarding Qualified Investors is applicable to it; (iii) that it will abide by all provisions set forth in the Israeli Securities Law, 5728-1968 and the regulations promulgated thereunder in connection with the offer to be issued common stock; (iv) that the shares of common stock that will be issued are, subject to exemptions available under the Israeli Securities Law, 5728-1968: (a) for its own account; (b) for investment purposes only; and (c) not issued with a view to resale within the State of Israel, other than in accordance with the provisions of the Israeli Securities Law, 5728-1968; and (v) that it is willing to provide further evidence of its Qualified Investor status. Addressed Investors may have to submit written evidence in respect of their identity and may have to sign and submit a declaration containing, inter alia, the Addressed Investor's name, address and passport number or Israeli identification number.

Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission ("ASIC"), in relation to the offering. This prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the "Corporations Act"), and does not purport to include the information required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the shares of common stock may only be made to persons (the "Exempt Investors") who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer the shares of common stock without disclosure to investors under Chapter 6D of the Corporations Act.

The shares of common stock applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under the offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring shares of common stock must observe such Australian on-sale restrictions.

This prospectus contains general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Latham & Watkins LLP. Certain legal matters will be passed upon for the underwriters by Ropes & Gray LLP.

EXPERTS

The consolidated financial statements of bluebird bio, Inc. ("the Company") appearing in the Company's Annual Report (Form 10-K) for the year ended December 31, 2021, and the effectiveness of the Company's internal control over financial reporting as of December 31, 2021, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon (which contains an explanatory paragraph describing conditions that raise substantial doubt about the Company's ability to continue as a going concern as described in Note 1 to the consolidated financial statements) included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file reports, proxy statements and other information with the SEC. The SEC maintains a web site that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. Information filed with the SEC is available on the SEC's website at http://www.sec.gov.

We are subject to the information reporting requirements of the Exchange Act, and we have filed and will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information are available on the SEC's website at http://www.sec.gov. We also maintain a website at www.bluebirdbio.com, at which you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated into, this prospectus supplement.

This prospectus supplement is part of a registration statement that we filed with the SEC and does not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. Statements in this prospectus supplement and the accompanying prospectus about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement through the SEC's website or our website, as provided above.

INCORPORATION BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement. Information in this prospectus supplement supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus supplement. We incorporate by reference into this prospectus supplement and the registration statement of which this prospectus supplement and the accompanying prospectus is a part the information or documents listed below that we have filed with the SEC:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the SEC on March 4, 2022;
- the information specifically incorporated by reference into our Annual Report on Form 10-K from our Definitive Proxy Statement on Schedule 14A, filed with the SEC on May 2, 2022;
- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2022, June 30, 2022 and September 30, 2022, filed with the SEC on <u>May 9, 2022, August 4, 2022</u> and <u>November 7, 2022</u>, respectively;
- our Current Reports on Form 8-K filed on January 18, 2022, February 4, 2022, March 4, 2022, March 7, 2022, March 31, 2022, April 5, 2022, May 2, 2022, June 7, 2022, June 10, 2022, June 10, 2022, June 22, 2022, June 23, 2022, August 4, 2022, August 17, 2022, September 12, 2022, September 12, 2022, November 7, 2022, November 7, 2022, December 12, 2022, December 12, 2022, January 3, 2023, and January 6, 2023, excluding, in each case, information "furnished" pursuant to Items 2.02, 7.01, or 9.01; and
- the description of our common stock contained in our registration statement on Form 8-A, filed with the SEC on June 14, 2013, including any amendment or report filed for the purpose of updating such description.

We are also incorporating by reference any future filings that we make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement.

Notwithstanding the statements in the preceding paragraphs, no document, report or exhibit (or portion of any of the foregoing) or any other information that we have "furnished" to the SEC pursuant to the Exchange Act shall be incorporated by reference into this prospectus supplement and the accompanying prospectus.

We will furnish without charge to you, on written or oral request, a copy of any or all of the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, including exhibits to these documents. You should direct any requests for documents either orally or in writing to:

bluebird bio, Inc. 455 Grand Union Boulevard Somerville, MA 02145 Phone: (339) 499-9300 investor@bluebirdbio.com Attn: Investor Relations

You also may access these filings on our website at www.bluebirdbio.com. We do not incorporate the information on our website into this prospectus supplement or the accompanying prospectus and you should not consider any information on, or that can be accessed through, our website as part of this prospectus supplement or any accompanying prospectus (other than those filings with the SEC that we specifically incorporate by reference into this prospectus supplement and the accompanying prospectus).

Any statement contained in a document incorporated or deemed to be incorporated by reference in this prospectus supplement will be deemed modified, superseded or replaced for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement modifies, supersedes or replaces such statement.

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, and in one or more series, common stock, preferred stock, warrants, units, 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 "<u>RISK FACTORS</u>" ON PAGE 4 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 February 18, 2020.

TABLE OF CONTENTS

4

11

11

ABOUT THIS PROSPECTUS
WHERE YOU CAN FIND ADDITIONAL INFORMATION
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS
<u>RISK FACTORS</u>
ABOUT THE COMPANY
DESCRIPTION OF SECURITIES
<u>USE OF PROCEEDS</u>
SELLING STOCKHOLDERS
PLAN OF DISTRIBUTION
LEGAL MATTERS
EXPERTS

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.

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 "wellknown 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, units, 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 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 supplement or any related free writing prospectus that we or a selling stockholder may authorize to be provided to you. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. 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" or 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

1

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, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

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, the "Exchange Act"), and, in accordance therewith, file annual, quarterly and special reports, proxy statements and other information with the SEC. These documents 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., 60 Binney Street, Cambridge, Massachusetts 02142, Attention: Secretary, or by telephone request to (339) 499-9300. Our website is located at *http://www.bluebirdbio.com.* Information contained on, or that can be accessed through, our website is not incorporated by reference into this prospectus and, therefore, is not part of this prospectus or any accompanying prospectus supplement.

INCORPORATION OF CERTAIN INFORMATION 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 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. 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 or in any document previously incorporated by reference have been modified or superseded. This prospectus 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 Exchange Act (in each case, other than those documents or the portions of those documents deemed to be furnished and not be filed in accordance with SEC rules) between the date of this prospectus and the termination of this offering:

- Annual Report on Form 10-K for the year ended December 31, 2019, as filed with the SEC on February 18, 2020;
- Current Reports on Form 8-K, as filed with the SEC on January 13, 2020 (solely with respect to item 8.01 and the associated Item 9.01 (Exhibit 99.2)), and January 21, 2020; and
- The description of our common stock contained in our registration statement on <u>Form 8-A</u>, 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:

bluebird bio, Inc. 60 Binney Street Cambridge, Massachusetts 02142 Phone: (617) 245-2107 investor@bluebirdbio.com Attn: Investor Relations

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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This 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 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 "may," "will," "could," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," 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 approved product and any future approved products;
- the pricing and reimbursement of our approved product and any future approved products;

- 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 approved product, 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" in any documents incorporated by reference herein.

Given these uncertainties, you should not place undue reliance on these 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 or the respective dates of documents incorporated by reference herein that include forward-looking statements.

RISK FACTORS

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 our most recent annual report on Form 10-K which is on file with the SEC and is incorporated herein by reference, we file with the SEC that are deemed incorporated by reference into this prospectus.

ABOUT THE COMPANY

We are a biotechnology company committed to researching, developing, and commercializing potentially transformative gene therapies for severe genetic diseases and cancer. We have built an integrated product platform with broad therapeutic potential in a variety of indications based on our lentiviral gene addition platform, gene editing and cancer immunotherapy capabilities. We believe that gene therapy for severe genetic diseases has the potential to change the way patients living with these diseases are treated by addressing the underlying genetic defect that is the cause of their disease, rather than offering treatments that only address their symptoms. Our gene therapy programs include LentiGlobin for b-thalassemia; LentiGlobin for sickle cell disease, or SCD; and Lenti-D for cerebral adrenoleukodystrophy, or CALD. Our programs in oncology are focused on developing novel T cell-based immunotherapies, including chimeric antigen receptor (CAR) and T cell receptor (TCR) T cell therapies. bb2121 (idecabtagene vicleucel), and bb21217 are CAR-T cell product candidates for the treatment of multiple myeloma and partnered under our collaboration arrangement with Bristol-Myers Squibb.

In June 2019, we received conditional marketing approval from the European Commission for LentiGlobin gene therapy for b-thalassemia, being marketed in the European Union as ZYNTEGLOTM gene therapy (autologous CD34+ cells encoding bA-T87Q-globin gene), for patients 12 years and older with transfusion-dependent b-thalassemia, or TDT, who do not have a b0/b0 genotype, for whom hematopoietic stem cell, or HSC, transplantation is appropriate, but a human leukocyte antigen-matched, or HLA, related HSC donor is not available. We have begun commercializing ZYNTEGLO in the European Union and expect to begin generating product revenue in the first half of 2020. In the fourth quarter of 2019, we initiated rolling submission of a biologics license application, or BLA, to the U.S. Food and Drug Administration, or FDA, for regulatory approval of LentiGlobin for b-thalassemia in the United States for the treatment of patients with TDT who do not have a b0/b0 genotype. We are engaged with the FDA in discussions regarding the requirements and timing for providing certain information regarding various release assays for LentiGlobin for b-thalassemia, and subject to these ongoing discussions, we are currently planning to complete the BLA submission in the second half of 2020. We are engaged with the FDA and the European Medicines Agency, or EMA, in discussions regarding our proposed development plans for LentiGlobin for b-thalassemia in patients with TDT and b0/b0 genotypes.

We are currently developing LentiGlobin gene therapy for SCD in the United States and the European Union. We are engaged with the FDA and EMA in discussions regarding our proposed development plans, and anticipate a potential first submission in 2022 for marketing approval of LentiGlobin for the treatment of patients with SCD on the basis of clinical data from our ongoing HGB-206 and HGB-210 studies.

We are currently developing Lenti-D gene therapy for CALD in the United States and the European Union. Based on our discussions with the FDA and EMA, we believe that we may be able to seek approval for our Lenti-D gene therapy for the treatment of patients with CALD on the basis of clinical data from our ongoing Starbeam study, and the completed ALD-103 observational study. We anticipate a potential first submission in 2020 for marketing approval of our Lenti-D gene therapy for the treatment of patients with CALD.

In collaboration with Bristol-Myers Squibb, or BMS, we are developing bb2121 (idecabtagene vicleucel, or ide-cel) and bb21217 product candidates as treatments for multiple myeloma. We are co-developing and co-promoting ide-cel in the United States with BMS and we have exclusively licensed to BMS the development and commercialization rights for ide-cel outside of the United States. We and BMS anticipate a potential first submission in the first half of 2020 for marketing approval of ide-cel as a treatment for relapsed and refractory multiple myeloma. We have exclusively licensed the development and commercialization rights for the bb21217 product candidate to BMS, with an option for us to elect to co-develop and co-promote bb21217 within the United States.

We also have the following programs to discover and develop T cell product candidates to treat hematologic and solid tumor malignancies: acute myeloid leukemia, Merkel cell carcinoma, diffuse large B-cell lymphoma, and MAGE-A4 positive solid tumors. In the field of severe genetic diseases, we have a preclinical program for a gene therapy to treat mucopolysaccharidosis type I (MPSI), a genetic ultra-rare metabolic condition that causes severe neurologic impairment and organ damage.

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 02142 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."

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.

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.

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.

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.

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.

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 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.

LEGAL MATTERS

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

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2019, and the effectiveness of our internal control over financial reporting as of December 31, 2019, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

20,000,000 Shares of Common Stock



Prospectus Supplement

Goldman Sachs & Co. LLC

J.P. Morgan

January 18, 2023

Calculation of Filing Fee Tables

424(b)(5) (Form Type)

bluebird bio, Inc. (Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial effective date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Fees to Be		Common										
Paid		Stock,										
		\$0.01										
	Equity	par value		23,000,000(1)	\$6.00	\$138,000,000.00	0.00011020	\$15 207 60(2)		_	_	
Fees	Equity	Per share	10,(1)	20,000,000(1)	\$5.00	#120,000,000.00	0.00011020	¢10,207.00(2)				
Previously												
Paid	—	—	—	—	_	—	—	_	—	—		
Carry Forward Securities												
Carry												
Forward												
Securities	—		—	—		—	—				—	—
	Total Offering Amounts					\$138,000,000.00		\$15,207.60				
	Total Fees Previously Paid											
	Total Fee Offsets											
	Net Fee Due							\$15,207.60				

(1) The amount registered includes shares of Common Stock that may be purchased by the underwriters pursuant to their option to purchase additional shares of Common Stock.

(2) The registration fee relates to the Registration Statement on Form S-3ASR (File No. 333-236489) filed by the Registrant on February 18, 2020.