The information in this preliminary prospectus supplement and the accompanying prospectus, relating to an effective registration statement under the Securities Act of 1933, as amended, is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, dated December 18, 2023

PRELIMINARY PROSPECTUS SUPPLEMENT (To Prospectus dated May 19, 2023)

\$150,000,000 of Shares of Common Stock



We are offering \$150,000,000 of shares of our common stock.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "BLUE." On December 15, 2023, the last reported sale price of the common stock on the Nasdaq Global Select Market was \$3.27 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 "Risk Factors" beginning on page S-6 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	\$	\$
Underwriting discounts and commissions(1)	\$	\$
Proceeds, before expenses, to us	\$	\$

(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 an additional \$22,500,000 of 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 \$ and the total proceeds to us, before expenses, will be \$.

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 , 2023.

Goldman Sachs & Co. LLC

J.P. Morgan

Raymond James

The date of this prospectus supplement is , 2023.

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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, 2022 and Quarterly Reports on Form 10-Q for the quarters ended March 31, 2023, June 30, 2023 and September 30, 2023, 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 ® and ™ 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-6 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 transformative gene therapies for severe genetic diseases based on our lentiviral vector gene addition platform. In 2022, following more than a decade of leadership in research and clinical development, we received approval from the U.S. Food and Drug Administration (the "FDA") for two gene therapies, both of which were recently launched, and in December 2023, we received approval from the FDA for a third gene therapy.

On August 17, 2022, ZYNTEGLO (betibeglogene autotemcel, also known as beti-cel), was approved by the FDA for the treatment of adult and pediatric patients with ß-thalassemia who require regular red blood cell transfusions. On September 16, 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. We received a Rare Pediatric Disease Priority Review Voucher in connection with each of the approvals of ZYNTEGLO and SKYSONA. On December 8, 2023, LYFGENIA (lovotibeglogene autotemcel, also known as lovo-cel), was approved by the FDA for the treatment of patients 12 years of age or older with sickle cell disease and a history of vaso-occlusive events. The LYFGENIA product label includes a boxed warning for the risk of hematologic malignancy. In connection with the approval of LYFGENIA, we did not receive a Rare Pediatric Disease Priority Review Voucher that we requested as part of the FDA's review. We are evaluating the FDA's denial and plan to dispute this decision with the FDA.

We have an established commercial infrastructure that is synergistic for LYFGENIA and ZYNTEGLO. Currently, there are 37 qualified treatment centers ("QTCs") activated (defined as a signed master service agreement) for ZYNTEGLO. Thirty QTCs are ready to receive referrals for patients for LYFGENIA. Additionally, we have put in place outcomes-based agreements for both ZYNTEGLO and LYFGENIA that provide payers with meaningful risk sharing tied to clinical outcomes that can be tracked in claims data.

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 \$150,000,000 of shares.

Common stock to be outstanding immediately after this shares (or shares if the underwriters exercise in full their option to offering purchase additional shares).

Option to purchase additional Shares of common stock The underwriters have a 30-day option to purchase up to an additional \$22,500,000 of

shares of our common stock at the public offering price less underwriting discounts and

commissions.

Use of proceeds We currently intend to use the net proceeds from this offering, together with our existing

cash, cash equivalents and marketable securities:

 to support commercialization and manufacturing for our three approved gene therapies, ZYNTEGLO, SKYSONA and LYFGENIA; 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-6 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 Equiniti Trust Company, LLC

The number of shares of common stock to be outstanding immediately after this offering is based on 107,022,138 shares of common stock outstanding as of September 30, 2023, and excludes:

• 5,874,722 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2023, at a weighted average exercise price of \$24.94 per share;

- 4,193,617 shares of common stock issuable upon the vesting of restricted stock units ("RSUs") outstanding as of September 30, 2023;
- 1,216,673 shares of common stock reserved for future issuance under our 2013 Employee Stock Purchase Plan (the "ESPP") as of September 30, 2023;
- 4,792,060 shares of common stock reserved for future issuance under our 2023 Incentive Award Plan (the "2023 Plan") as of September 30, 2023;
- 1,099,423 shares of common stock reserved for future issuance under our 2021 Inducement Plan (the "Inducement Plan") as of September 30, 2023; and

• 2,272,727 shares of common stock reserved for future issuance upon exercise of pre-funded warrants outstanding as of September 30, 2023, which were exercised in full in October 2023.

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 or vesting of the outstanding 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, 2022 and Quarterly Report on Form 10-Q for the quarter ended September 30, 2023, 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 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 approximately \$ per share. Furthermore, if outstanding options 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 our three approved gene therapies, ZYNTEGLO, SKYSONA and LYFGENIA, 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.

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, 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.

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 commercial programs, product development efforts or other operations.

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, 2023, we expect

that our Annual Report on Form 10-K for the fiscal year ended December 31, 2023, when filed with the Securities and Exchange Commission, and the report of our auditors contained therein, whether or not this offering is successful, may reflect there is substantial doubt regarding our ability to continue as a going concern for a period of one year after such date. Accordingly, we will need to raise additional funding in order to execute on our current business plans and strategy, including prior to becoming profitable.

Our efforts to raise additional funding may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our 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, traditional debt or other debt-like arrangements, 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.

Moreover, as a result of recent volatile market conditions, the cost and availability of capital has been and may continue to be adversely affected. Concern about the stability of the banking sector has generally led many lenders and institutional investors to reduce, and in some cases, cease to provide credit to businesses and consumers. Continued turbulence in the U.S. market and economy may adversely affect our liquidity and financial condition, including our ability to access the capital markets to meet liquidity needs. In addition, we maintain the majority of our cash and cash equivalents in accounts with major financial institutions, and our deposits at these institutions exceed insured limits. Market conditions can impact the viability of these institutions. In the event of failure of any of the financial institutions where we maintain our cash and cash equivalents, there can be no assurance that we would be able to access uninsured funds in a timely manner or at all. Any inability to access or delay in accessing these funds could adversely affect our business and financial position.

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 the commercialization of any current or future products 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.

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. As

of November 30, 2023, we had 109,408,603 shares of common stock outstanding. 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

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Sections 382 and 383 of the U.S. Internal Revenue Code of 1986, as amended (the "Code"), if a corporation undergoes an "ownership change," generally defined as a cumulative change of greater than 50% (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards ("NOLs") and other pre-change tax attributes (such as research and development tax credits) to offset its post-change income and taxes may be limited. We have completed several financings since our inception, which we believe have resulted in shifts in our equity ownership. We completed a study through December 2020 confirming no ownership changes have occurred since our initial public offering in 2013. We may have experienced ownership changes since December 2020, and we may also experience ownership changes in the future, as a result of subsequent shifts in our equity ownership, some of which are outside our control. There is a significant likelihood that we may experience an ownership change as a result of this offering, although whether we experience an ownership change as a result of this offering will depend on the specific facts that apply at the time of the offering. If finalized, Treasury Regulations currently proposed under Section 382 of the Code may further limit our ability to utilize our pre-change NOLs or other pre-change tax attributes if we undergo a future ownership change. Accordingly, if we earn net taxable income, our ability to use our pre-change NOLs and other pre-change tax attributes to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs and other pre-change tax attributes is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

Risks related to commercialization

The commercial success of ZYNTEGLO, SKYSONA and LYFGENIA will depend upon the degree of market acceptance by physicians, patients, payers and other stakeholders.

The commercial success of ZYNTEGLO, SKYSONA, and LYFGENIA will depend in part on the medical community, patients, and third-party or governmental payers accepting gene therapy products in general, and ZYNTEGLO, SKYSONA, and LYFGENIA, in particular, as medically useful, cost-effective, and safe. ZYNTEGLO, SKYSONA, and LYFGENIA may not gain market acceptance by physicians, patients, payers and other stakeholders. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of ZYNTEGLO, SKYSONA, and LYFGENIA will depend on a number of factors, including:

- the potential and perceived efficacy and potential advantages over alternative treatments, including over direct competitors in the gene therapy space;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling; for
 instance, each of the SKYSONA and LYFGENIA product labels includes a boxed warning for the risk of hematologic malignancy;
- the prevalence and severity of any side effects resulting from the chemotherapy and myeloablative treatments associated with the procedure by which our products are administered, including the possible prejudicial effects that chemotherapy can have on fertility;
- relative convenience and ease of administration;
- given the complexity of manufacturing product and the reduced operational success rates in connection with the transition to commercial manufacturing, the perception or possibility that issues may continue to arise in the supply of product which could delay treatment;

- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- the pricing of our products;
- publicity concerning our products, or competing products and treatments;
- sufficient insurance coverage or reimbursement;
- the possible occurrence of adverse clinical findings or decreased effectiveness of a product or product candidate over time identified during continued monitoring and evaluation of patients; and
- the mix of private and governmental payers coverage, particularly if the percentage of patients receiving reimbursement from state Medicaid is high since such process can be slower to reimburse.

Even if a product displays a favorable efficacy and safety profile in clinical studies, market acceptance of the product will not be known until some period after it is launched. Our efforts to educate the medical community and payers on the benefits of our products may require significant resources and may never be successful. For instance, following marketing approval of ZYNTEGLO in the European Union, we did not reach agreement with payers on an acceptable price for reimbursement in our priority markets in Europe, and as a result we are no longer seeking to commercialize our products and product candidates in Europe for the foreseeable future. Our efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors. Any of these factors may cause ZYNTEGLO, SKYSONA, or LYFGENIA to be unsuccessful or less successful than anticipated.

Risks related to the research and development of our product candidates

We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are more advanced, safer, less expensive or more effective than ours, which may adversely affect our financial condition and our ability to successfully develop and commercialize ZYNTEGLO, SKYSONA and LYFGENIA.

We are engaged in the development of gene therapies for severe genetic diseases, which is a competitive and rapidly-changing field. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff, more experienced manufacturing capabilities, or more established commercial infrastructure. For instance, the FDA has approved a gene therapy for the treatment of sickle cell disease from Vertex Pharmaceuticals, Inc. ("Vertex") and we are aware that the FDA has accepted a BLA submitted by Vertex for a gene therapy for the treatment of beta thalassemia. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products that are more effective, safer, or less costly than any products that we may develop, or achieve patent protection, marketing approval, product commercialization and market penetration earlier than us. For example, Vertex's approved gene therapy for sickle cell disease does not have a boxed warning and its wholesale acquisition cost in the United States is lower than that of LYFGENIA. Additionally, technologies developed by our competitors may render our products or product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

Finally, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity and/or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

Risks related to our financial condition and capital requirements

Amounts under our factoring arrangement are subject to terms that may adversely affect our operations and financial condition.

We entered into an accounts receivable factoring agreement in December 2023. The factoring agreement provides for us to have access to up to \$100,000,000.00 on a revolving basis, measured by the outstanding balance of purchased accounts from time to time. Upon receipt of the upfront purchase price for any purchased accounts, we will have sold and assigned all of our rights in such purchased accounts and all proceeds thereof. The buyer has the right to require that we repurchase any purchased account that was ineligible as of the date of purchase or with respect to which any account debtor asserts a dispute that is not resolved by the related due date. The buyer does not have recourse to us for the insolvency or other credit risk of the account debtors. We have granted the buyer a security interest in the purchased accounts, and proceeds thereof, as more fully described in the agreement, in order to perfect the buyer's ownership interest in the purchased accounts and secure the payment and performance of all our obligations to the buyer under the agreement. If the buyer demands repurchase and we fail to do so, or if we cause or permit any other event of default as defined in the agreement, or fail to comply with covenants set forth in the agreement, we would be subject to additional expenses and lose access to this agreement to fund further accounts receivable. Such results could have a material adverse effect on our operations and financial condition.

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," "continue," "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 advance product candidates into, and successfully complete, clinical studies;
- our ability to obtain adequate financing to fund our operations and to execute on our strategy;
- our expectations and projections regarding the sufficiency of our cash, cash equivalents and marketable securities and restricted cash to fund our operations;
- 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, and our plans and expectations regarding our manufacturing activities;
- the timing or likelihood of regulatory filings and marketing approvals for our product candidates and our plans and expectations relating thereto;
- our plans and expectations regarding our commercialization activities for any approved products and the timing or success thereof, including expectations regarding our network of qualified treatment centers;
- 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, 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;
- developments relating to our competitors and our industry;
- the impact of the general economic conditions and uncertainties;
- 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-6 of this prospectus supplement, in "Item 1A. Risk Factors" in our Annual Report on Form 10-K for the fiscal year ended December 31, 2022, in "Item 1A. Risk Factors" in our Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2023 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 estimated underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$\text{million}\$ million (or approximately \$\text{million}\$ 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, cash equivalents and marketable securities:

- · to support commercialization and manufacturing for our three approved gene therapies, ZYNTEGLO, SKYSONA and LYFGENIA; 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.

Based on our current business plan, we anticipate that our cash, cash equivalents, and marketable securities excluding restricted cash, together with the net proceeds of this offering for not less than \$150 million of gross proceeds, and anticipated cash flows from operations (taking into account the effect of an accounts receivable-backed factoring agreement), will be sufficient to fund our operations into the first quarter of 2025. Our expectations regarding our anticipated cash runway into the first quarter of 2025 will be affected by many factors, including our ability to raise \$150 million in gross proceeds from this offering, our ability to execute our current business plan, the ongoing commercialization of our three approved products, the number of patient starts for our three approved products, and our realization of anticipated revenue. These expectations are based on estimates and the judgment of management. Our cash runway may not extend as far as we have forecast and anticipated cash needs could be greater than we expect. See "Risk Factors—Risks related to this offering—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 commercial programs, product development efforts or other operations."

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, 2023 was approximately \$211.5 million, or approximately \$1.98 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 107,022,138 shares of common stock outstanding as of September 30, 2023.

After giving effect to the sale of shares of our common stock in this offering, and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2023 would have been approximately \$ million, or approximately \$ per share. This represents an immediate increase in net tangible book value of \$ per share to existing stockholders and immediate dilution in net tangible book value of \$ 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		\$
Historical net tangible book value per share as of September 30, 2023	\$1.98	
Increase in as adjusted net tangible book value per share attributable to this		
offering		
Pro forma as adjusted net tangible book value per share after this offering	·	
Dilution per share to new investors purchasing common stock in this offering		\$

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

The above table is based on 107,022,138 shares of common stock outstanding as of September 30, 2023, and excludes as of that date:

- 5,874,722 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2023, at a weighted average exercise price of \$24.94 per share;
- 4,193,617 shares of common stock issuable upon the vesting of RSUs outstanding as of September 30, 2023;
- 4,792,060 shares of common stock reserved for future issuance under our 2023 Plan as of September 30, 2023;
- 1,216,673 shares of common stock reserved for future issuance under our ESPP as of September 30, 2023;
- 1,099,423 shares of common stock reserved for future issuance under our Inducement Plan as of September 30, 2023; and
- 2,272,727 shares of common stock reserved for future issuance upon exercise of pre-funded warrants outstanding as of September 30, 2023, which were exercised in full in October 2023.

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 (the "Code"), Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service (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. Holders 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(l)(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 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 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 ("USRPI"), by reason of our status as a U.S. real property holding corporation ("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 withheld 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 ("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 our common stock beginning on 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.

	Number of
<u>Underwriters</u>	Shares of Common Stock
Goldman Sachs & Co. LLC	
J.P. Morgan Securities LLC	
Raymond James & Associates, Inc.	
Total	

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 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 additional shares.

Paid by the Company	No Exercise	Full Exercise
Per Share of Common Stock	\$	\$
Total	\$	S

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 \$ 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 certain limited exceptions), 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; and
- the issuance by us of shares issued in connection with a transaction with an unaffiliated third party that includes a bona fide commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or not less than a majority or controlling portion of the equity of another entity; provided that the aggregate number of shares issued shall not exceed ten percent of the total number of outstanding shares of our common stock immediately following this offering; provided further that the recipient of any such shares during the 60-day restricted period described above shall enter into an agreement providing for transfer restrictions as set forth above.

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

In connection with the offering, the underwriters may purchase and sell shares of common stock in the open market. These transactions may include short sales, stabilizing transactions and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering, and a short position represents the amount of such sales that have not been covered by subsequent purchases. A "covered short position" is a short position that is not greater than the amount of additional shares for which the underwriters' option described above may be exercised. The underwriters may cover any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to cover the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase additional shares pursuant to the option described above. "Naked" short sales are any short sales that create a short position greater than the amount of additional shares for which the option described above may be exercised. The underwriters must cover any such naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of common stock made by the underwriters in the open market prior to the completion of the offering.

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

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

The Company may enter into derivative transactions with third parties, or sell securities not covered by this prospectus 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;
- (ii) 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's securities pursuant to Section 275(1A) of the SFA, (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 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 \$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 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, 2022 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report 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, 2022, filed with the SEC on March 29, 2023;
- 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 <u>April 28, 2023</u>;
- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2023, June 30, 2023 and September 30, 2023, filed with the SEC on May 9, 2023, August 8, 2023 and November 7, 2023, respectively;
- our Current Reports on Form 8-K filed on <u>January 3, 2023</u>, <u>January 6, 2023</u>, <u>January 19, 2023</u>, <u>March 29, 2023</u>, <u>June 20, 2023</u>, <u>August 8, 2023</u>, <u>September 27, 2023</u>, <u>October 30, 2023</u>, <u>December 11, 2023</u> and <u>December 18, 2023</u>, 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 <u>June 14, 2013</u>, 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



\$350,000,000

Common Stock Preferred Stock Debt Securities Warrants Units

We may offer and sell up to \$350,000,000 in the aggregate of the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE "RISK FACTORS" ON PAGE 7 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on the Nasdaq Global Select Market under the symbol "BLUE." On May 5, 2023, the last reported sale price of our common stock on the Nasdaq Global Select Market was \$4.37 per share.

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

The date of this prospectus is May 19, 2023.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, using a "shelf" registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings up to a total dollar amount of \$350,000,000 as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that 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. The prospectus supplement or free writing prospectus may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading "Where You Can Find More Information; Incorporation by Reference."

We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, and that any information incorporated by reference is accurate only as of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates. This prospectus incorporates by reference, and any prospectus supplement or free writing prospectus may contain and incorporate by reference, market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. In addition, the market and industry data and forecasts that may be included or incorporated by reference in this prospectus, any prospectus supplement or any applicable free writing prospectus may involve estimates, assumptions and other risks and uncertainties and are subject to change based on various factors, including those discussed under the heading "Risk Factors" contained in this prospectus, the applicable prospectus supplement and any applicable free writing prospectus, a

When we refer to "bluebird," "we," "our," "us" and the "Company" in this prospectus, we mean bluebird bio, Inc. and its consolidated subsidiaries, unless otherwise specified. When we refer to "you," we mean the potential holders of the applicable series of securities.

This prospectus 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 appear without the [®] and [™] 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance. All statements other than statements of historical facts contained in this prospectus are forward-looking statements. These statements involve known and unknown risks, uncertainties, and other important 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 the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "should," "expects," "might," "plans," "anticipates," "could," "intends," "target," "projects," "contemplates," "believes," "estimates," "predicts," "potential," "seek," "would" or "continue," or the negative of these terms or other similar expressions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Some of the key factors that could cause actual results to differ from our expectations include, but are not limited to, the following:

- 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 obtain adequate financing to fund our operations and to execute on our strategy;
- our expectations and projections regarding the sufficiency of our cash, cash equivalents, marketable securities and restricted cash to fund our operations;
- 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, and our plans and expectations regarding our manufacturing activities;
- the timing or likelihood of regulatory filings and marketing approvals for our product candidates and our plans and expectations relating thereto;
- our plans and expectations regarding our commercialization activities for any approved products and the timing or success thereof, including expectations regarding our network of qualified treatment centers;
- 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, 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;

- developments relating to our competitors and our industry;
- the impact of the general economic conditions and uncertainties, including as a result of the COVID-19 pandemic; and
- other risks and uncertainties, including those listed under "Risk Factors" on page 7 of this prospectus and any similar section contained in the applicable prospectus supplement.

WHERE YOU CAN FIND MORE INFORMATION: INCORPORATION BY REFERENCE

Available 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. The address of that website is http://www.sec.gov.

Our web site address is https://www.bluebirdbio.com. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and do 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. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement or documents incorporated by reference in the registration statement. Statements in this prospectus or any prospectus supplement 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, as provided above.

Incorporation by Reference

The SEC's rules allow us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in this prospectus or a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or a subsequently filed document incorporated by reference modifies or replaces that statement.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

- Our Annual Report on Form 10-K for the year ended December 31, 2022, filed with the SEC on March 29, 2023.
- The information specifically incorporated by reference into our Annual Report on Form 10-K from our <u>Definitive Proxy Statement</u> on Schedule 14A, filed with the SEC on April 28, 2023.
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2023, filed with the SEC on May 9, 2023.
- Our Current Reports on Form 8-K filed with the SEC on <u>January 3, 2023, January 6, 2023, January 19, 2023</u> and <u>March 29, 2023</u>, excluding, in each case, information "furnished" pursuant to Items 2.02, 7.01, or 9.01.
- The description of our Common Stock contained in the our registration statement on <u>Form 8-A</u> filed with the SEC on June 14, 2013 and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the "Exchange Act" in this prospectus, prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any

information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus by writing or telephoning us at the following address:

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

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus or any accompanying prospectus supplement.

THE COMPANY

We are a biotechnology company committed to researching, developing, and commercializing potentially curative transformative gene therapies for severe genetic diseases based on our lentiviral vector ("LVV") gene addition platform. In 2022, following more than a decade of leadership in research and clinical development, we received approval from the U.S. Food and Drug Administration (the "FDA") for two gene therapies, both of which were recently launched.

On August 17, 2022, ZYNTEGLO (betibeglogene autotemcel, also known as beti-cel), was approved by the FDA for the treatment of adult and pediatric patients with \(\beta\)-thalassemia who require regular red blood cell transfusions. On September 16, 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"). On April 24, 2023, we announced that we had submitted a biologics licensing application ("BLA") to the FDA for our third gene therapy candidate – lovotibeglogene autotemcel – also known as lovo-cel – requesting priority review of the treatment for patients 12 and older with sickle cell disease ("SCD") with a history of vaso-occlusive-events.

We filed our original certificate of incorporation with the Secretary of State of Delaware on April 16, 1992.

Our principal executive offices are located at 455 Grand Union Boulevard, Somerville, MA 02145, and our telephone number is (339) 499-9300.

RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. Before deciding whether to invest in our securities, you should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement and any applicable free writing prospectus. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our securities to decline, resulting in a loss of all or part of your investment. Please also carefully read the section entitled "Forward-Looking Statements" included in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our certificate of incorporation, which has been publicly filed with the SEC. See "Where You Can Find More Information; Incorporation by Reference."

Our authorized capital stock consists of:

- 125,000,000 shares of common stock, par value \$0.01 per share; and
- 5,000,000 shares of preferred stock, par value \$0.01 per share.

Common Stock

We 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.

Transfer Agent

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

Dividend

We have not paid any cash dividends on our common stock since inception and do not anticipate paying cash dividends in the foreseeable future.

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.

Anti-Takeover Effects of Delaware Law

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. Under Section 203, we would generally be prohibited from engaging in any business combination with any interested stockholder for a period of three years following the time that this stockholder became an interested stockholder unless:

- prior to this time, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding shares owned by persons who are directors and also officers, and by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to such time, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Under Section 203, a "business combination" includes:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder, subject to limited exceptions;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by such entity or person.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement or free writing prospectus, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee to be named in the applicable indenture, as trustee. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

As used in this section only, "bluebird," "we," "our" or "us" refer to bluebird bio, Inc. excluding our subsidiaries, unless expressly stated or the context otherwise requires.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet)

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

- the title and ranking of the debt securities (including the terms of any subordination provisions);
- the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;
- any limit on the aggregate principal amount of the debt securities;
- the date or dates on which the principal of the securities of the series is payable;
- the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;
- the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;

- the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities:
- any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and in the terms and conditions upon which securities of the series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;
- the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;
- the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;
- whether the debt securities will be issued in the form of certificated debt securities or global debt securities;
- the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;
- the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;
- the designation of the currency, currencies or currency units in which payment of principal of, premium and interest on the debt securities will be made;
- if payments of principal of, premium or interest on the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;
- the manner in which the amounts of payment of principal of, premium, if any, or interest on the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;
- any provisions relating to any security provided for the debt securities;
- any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;
- any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;
- any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;
- the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;
- any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and
- whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of and any premium and interest on any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company, or the Depositary, or a nominee of the Depositary (we will refer to any debt security represented by a global debt security as a "book-entry debt security"), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a "certificated debt security") as set forth in the applicable prospectus supplement. Except as set forth under the heading "Global Debt Securities and Book-Entry System" below, bookentry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depositary, and registered in the name of the Depositary or a nominee of the Depositary. Please see "Global Securities."

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a "successor person") unless:

- we are the surviving entity or the successor person (if other than bluebird) is a corporation, partnership, trust or other entity organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture; and
- · immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

"Event of Default" means with respect to any series of debt securities, any of the following:

- default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);
- default in the payment of principal of any security of that series at its maturity;
- default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or bluebird and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;
- · certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of bluebird;
- any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement.
 (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid

interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

- that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series;
 and
- the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, premium and any interest on that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each Securityholder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

to cure any ambiguity, defect or inconsistency;

- to comply with covenants in the indenture described above under the heading "Consolidation, Merger and Sale of Assets";
- to provide for uncertificated securities in addition to or in place of certificated securities;
- to add guarantees with respect to debt securities of any series or secure debt securities of any series;
- to surrender any of our rights or powers under the indenture;
- to add covenants or events of default for the benefit of the holders of debt securities of any series;
- to comply with the applicable procedures of the applicable depositary;
- to make any change that does not adversely affect the rights of any holder of debt securities;
- to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;
- to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or
- to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

- · reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;
- reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;
- reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to any series of debt securities;
- reduce the principal amount of discount securities payable upon acceleration of maturity;
- waive a default in the payment of the principal of, premium or interest on any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);
- make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;
- make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, premium and interest on those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or
- waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of

the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the irrevocable deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

- we may omit to comply with the covenant described under the heading "Consolidation, Merger and Sale of Assets" and certain other
 covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement;
 and
- any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series ("covenant defeasance").

The conditions include:

- depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and
- delivering to the trustee an opinion of counsel to the effect that the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

No Personal Liability of Directors, Officers, Employees or Securityholders

None of our past, present or future directors, officers, employees or securityholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the securities, will be governed by the laws of the State of New York.

The indenture will provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably waive, to the fullest extent permitted by applicable law, any and all right to trial by jury in any legal proceeding arising out of or relating to the indenture, the debt securities or the transactions contemplated thereby.

The indenture will provide that any legal suit, action or proceeding arising out of or based upon the indenture or the transactions contemplated thereby may be instituted in the federal courts of the United States of America located in the City of New York or the courts of the State of New York in each case located in the City of New York, and we, the trustee and the holder of the debt securities (by their acceptance of the debt securities) irrevocably submit to the non-exclusive jurisdiction of such courts in any such suit, action or proceeding. The indenture will further provide that service of any process, summons, notice or document by mail (to the extent allowed under any applicable statute or rule of court) to such party's address set forth in the indenture will be effective service of process for any suit, action or other proceeding brought in any such court. The indenture will further provide that we, the trustee and the holders of the debt securities (by their acceptance of the debt securities) irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the courts specified above and irrevocably and unconditionally waive and agree not to plead or claim any such suit, action or other proceeding has been brought in an inconvenient forum. (Section 10.10)

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

- the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;
- the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;
- the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;
- the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable:
- the terms of any rights to redeem or call the warrants;
- the date on which the right to exercise the warrants will commence and the date on which the right will expire;
- United States Federal income tax consequences applicable to the warrants; and
- any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

- to vote, consent or receive dividends;
- · receive notice as shareholders with respect to any meeting of shareholders for the election of our directors or any other matter; or
- exercise any rights as shareholders of bluebird.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any

other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any 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 agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

- the title of the series of units;
- identification and description of the separate constituent securities comprising the units;
- the price or prices at which the units will be issued;
- the date, if any, on and after which the constituent securities comprising the units will be separately transferable;
- a discussion of certain United States federal income tax considerations applicable to the units; and
- any other terms of the units and their constituent securities.

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, the securities initially will be issued in bookentry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, as depositary, or DTC, and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depositary to its nominee or by the nominee to the depositary, or by the depositary or its nominee to a successor depositary or to a nominee of the successor depositary.

DTC has advised us that it is:

- a limited-purpose trust company organized under the New York Banking Law;
- a "banking organization" within the meaning of the New York Banking Law;
- a member of the Federal Reserve System;
- a "clearing corporation" within the meaning of the New York Uniform Commercial Code; and
- a "clearing agency" registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants' accounts, thereby eliminating the need for physical movement of securities certificates. "Direct participants" in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC's records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants' records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC's partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC's records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depositary and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depositary or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below and unless if otherwise provided in the description of the applicable securities herein or in the applicable prospectus supplement, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in "street name." Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility, disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depositary with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depositary is not obtained, securities certificates are required to be printed and delivered.

As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

- DTC notifies us that it is unwilling or unable to continue as a depositary for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depositary is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;
- we determine, in our sole discretion, not to have such securities represented by one or more global securities; or
- an Event of Default has occurred and is continuing with respect to such series of securities,

we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depositary directs. It is expected that these directions will be based upon directions received by the depositary from its participants with respect to ownership of beneficial interests in the global securities.

Euroclear and Clearstream

If so provided in the applicable prospectus supplement, you may hold interests in a global security through Clearstream Banking S.A., which we refer to as "Clearstream," or Euroclear Bank S.A./N.V., as operator of the Euroclear System, which we refer to as "Euroclear," either directly if you are a participant in Clearstream or Euroclear or indirectly through organizations which are participants in Clearstream or Euroclear. Clearstream and Euroclear will hold interests on behalf of their respective participants through customers' securities accounts in the names of Clearstream and Euroclear, respectively, on the books of their respective U.S. depositaries, which in turn will hold such interests in customers' securities accounts in such depositaries' names on DTC's books.

Clearstream and Euroclear are securities clearance systems in Europe. Clearstream and Euroclear hold securities for their respective participating organizations and facilitate the clearance and settlement of securities transactions between those participants through electronic book-entry changes in their accounts, thereby eliminating the need for physical movement of certificates.

Payments, deliveries, transfers, exchanges, notices and other matters relating to beneficial interests in global securities owned through Euroclear or Clearstream must comply with the rules and procedures of those systems. Transactions between participants in Euroclear or Clearstream, on one hand, and other participants in DTC, on the other hand, are also subject to DTC's rules and procedures.

Investors will be able to make and receive through Euroclear and Clearstream payments, deliveries, transfers and other transactions involving any beneficial interests in global securities held through those systems only on days when those systems are open for business. Those systems may not be open for business on days when banks, brokers and other institutions are open for business in the United States.

Cross-market transfers between participants in DTC, on the one hand, and participants in Euroclear or Clearstream, on the other hand, will be effected through DTC in accordance with the DTC's rules on behalf of Euroclear or Clearstream, as the case may be, by their respective U.S. depositaries; however, such cross-market transactions will require delivery of instructions to Euroclear or Clearstream, as the case may be, by the counterparty in such system in accordance with the rules and procedures and within the established deadlines (European time) of such system. Euroclear or Clearstream, as the case may be, will, if the transaction meets its settlement requirements, deliver instructions to its U.S. depositary to take action to effect final settlement on its behalf by delivering or receiving interests in the global securities through DTC, and making or receiving payment in accordance with normal procedures for same-day fund settlement. Participants in Euroclear or Clearstream may not deliver instructions directly to their respective U.S. depositaries.

Due to time zone differences, the securities accounts of a participant in Euroclear or Clearstream purchasing an interest in a global security from a direct participant in DTC will be credited, and any such crediting will be reported to the relevant participant in Euroclear or Clearstream, during the securities settlement processing day (which must be a business day for Euroclear or Clearstream) immediately following the settlement date of DTC. Cash received in Euroclear or Clearstream as a result of sales of interests in a global security by or through a participant in Euroclear or Clearstream to a direct participant in DTC will be received with value on the settlement date of DTC but will be available in the relevant Euroclear or Clearstream cash account only as of the business day for Euroclear or Clearstream following DTC's settlement date.

Other

The information in this section of this prospectus concerning DTC, Clearstream, Euroclear and their respective book-entry systems has been obtained from sources that we believe to be reliable, but we do not take responsibility for this information. This information has been provided solely as a matter of convenience. The rules and procedures of DTC, Clearstream and Euroclear are solely within the control of those organizations and could change at any time. Neither we nor the trustee nor any agent of ours or of the trustee has any control over those entities and none of us takes any responsibility for their activities. You are urged to contact DTC, Clearstream and Euroclear or their respective participants directly to discuss those matters. In addition, although we expect that DTC, Clearstream and Euroclear will perform the foregoing procedures, none of them is under any obligation to perform or continue to perform such procedures and such procedures may be discontinued at any time. Neither we nor any agent of ours will have any responsibility for the performance or nonperformance by DTC, Clearstream and Euroclear or their respective participants of these or any other rules or procedures governing their respective operations.

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;
- at market prices prevailing at the time of sale;
- · at prices related to such prevailing market prices; or
- at negotiated prices.

Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any common stock will be listed on the Nasdaq Global Select Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising

their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us 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 and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

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

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

LEGAL MATTERS

Latham & Watkins LLP will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of bluebird bio, Inc. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of bluebird bio, Inc. appearing in bluebird bio, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2022, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report 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.

\$150,000,000 of Shares of Common Stock



Prospectus Supplement

Goldman Sachs & Co. LLC

Raymond James

J.P. Morgan

, 2023