

PROSPECTUS SUPPLEMENT to Prospectus dated February 13, 2020

**UP TO \$300,000,000****COMMON STOCK**

We have entered into a Sales Agreement with Cowen and Company, LLC, or Cowen, relating to shares of our common stock, par value \$0.001 per share, offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the Sales Agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$300,000,000 from time to time through Cowen, acting as sales agent or principal.

Our common stock is listed on the Nasdaq Global Select Market under the symbol “BPMC”. The last reported sales price of our common stock on the Nasdaq Global Select Market on February 15, 2022 was \$83.21 per share.

Investing in our common stock involves a high degree of risk. See “Risk Factors” beginning on page S-9 of this prospectus supplement, as well as in the documents incorporated or deemed to be incorporated by reference into this prospectus supplement and the accompanying prospectus, for a discussion of the factors you should carefully consider before deciding to purchase our common stock.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Cowen is not required to sell any specific number or dollar amount of securities, but will act as a sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Under the sales agreement, we may also sell shares of common stock to Cowen as principal for its own account, at a price to be agreed upon at the time of sale. If we sell shares to a Cowen as principal, we will enter into a separate terms agreement with Cowen, and we will describe the agreement in a separate prospectus supplement or pricing supplement.

The compensation to Cowen for sales of common stock sold pursuant to the Sales Agreement will be up to 3.0% of the gross proceeds of any shares of common stock sold under the Sales Agreement. In connection with the sale of the common stock on our behalf, Cowen will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation to Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act. See section titled “Plan of Distribution” on page S-15 of this prospectus supplement.

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

COWEN

The date of this prospectus supplement is February 17, 2022.

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

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement is part of an automatic shelf registration statement on Form S-3ASR (File No. 333-236424) that we filed with the Securities and Exchange Commission, or SEC, as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act, using a “shelf” registration process. Under this shelf registration process, we may, from time to time, sell any combination of the securities described in the above-referenced registration statement. This prospectus supplement, together with the accompanying prospectus and the documents incorporated by reference therein and herein, includes all material information relating to this offering.

This prospectus supplement relates to the offering of our common stock. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated by reference as described under the headings “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this prospectus supplement, and any accompanying prospectus or free writing prospectus that we have authorized for use in connection with this offering. These documents contain important information that you should consider when making your investment decision. This Sales Agreement prospectus is deemed a prospectus supplement to the base prospectus contained in the registration statement of which this Sales Agreement prospectus forms a part.

This prospectus supplement describes the terms of this offering of common stock and also adds to and updates information contained in the documents incorporated by reference into the accompanying prospectus. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in any document incorporated by reference into this prospectus supplement and the accompanying prospectus that was filed with the SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference into this prospectus supplement — the statement in the document having the later date modifies or supersedes the earlier statement.

We have not, and Cowen has not, authorized anyone to provide you with information in addition to or different from that contained in this prospectus supplement, the accompanying prospectus and any related free writing prospectus. We and Cowen take no responsibility for, and can provide no assurances as to the reliability of, any information not contained in this prospectus supplement, the accompanying prospectus or any related free writing prospectus that we may authorize to be provided to you. This prospectus supplement is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus supplement, the accompanying prospectus or any related free writing prospectus is accurate only as of the date on the front of the document and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus or any related free writing prospectus, or any sale of a security.

We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock 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.

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

Unless otherwise stated, all references in this prospectus supplement or the accompanying prospectus to “us”, “our”, “Blueprint”, “Blueprint Medicines”, “we”, the “Company” and similar designations refer, collectively, to Blueprint Medicines Corporation, a Delaware corporation, and its consolidated subsidiaries.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC’s website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.blueprintmedicines.com. Our website is not a part of this prospectus supplement and is not incorporated by reference in this prospectus supplement.

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiary and the securities we are offering. Statements in this prospectus supplement concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC’s website.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement is considered to be part of this prospectus supplement. Because we are incorporating by reference future filings with the SEC, this prospectus supplement is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement incorporates by reference the documents listed below (File No. 001-37359) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

- [Annual Report on Form 10-K for the fiscal year ended December 31, 2021, which was filed with the SEC on February 17, 2022;](#)
- The information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2021 from our [definitive proxy statement \(other than information furnished rather than filed\) for the 2021 Annual Meeting of Stockholders, which was filed with the SEC on April 21, 2021;](#)
- Current Reports on Form 8-K filed on [January 5, 2022](#) (solely with respect to Item 5.02), [January 10, 2022](#) (solely with respect to Item 8.01 and the information included in Exhibit 99.2) and [January 20, 2022](#) (solely with respect to Item 5.02); and
- [The description of our common stock contained in our Registration Statement on Form 8-A filed on April 27, 2015, including any amendments or reports filed for the purpose of updating such description.](#)

Notwithstanding the foregoing, unless specifically stated to the contrary, information that we furnish (and that is not deemed “filed” with the SEC) under Items 2.02 and 7.01 of any Current Report on Form 8-K, including the related exhibits under Item 9.01, is not incorporated by reference into this prospectus supplement or the registration statement of which this prospectus supplement is a part.

Any statement contained in a document that is incorporated by reference will be modified or superseded for all purposes to the extent that a statement contained in this prospectus supplement, or in any other

document that is subsequently filed with the SEC and incorporated by reference into this prospectus supplement, modifies or is contrary to that previous statement. Any statement so modified or superseded will not be deemed a part of this prospectus supplement, except as so modified or superseded. Since information that we later file with the SEC will update and supersede previously incorporated information, you should look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement or in any documents previously incorporated by reference have been modified or superseded.

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

Blueprint Medicines Corporation
45 Sidney Street
Cambridge, Massachusetts 02139
Attn: Investor Relations
Phone: (617) 714-6674
E-mail: ir@blueprintmedicines.com

You may also access these documents, free of charge on the SEC's website at www.sec.gov or on our website at www.blueprintmedicines.com. Information contained on our website is not incorporated by reference into this prospectus supplement and you should not consider any information on, or that can be accessed from, our website as part of this prospectus supplement.

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

You should rely only on the information incorporated by reference or provided in this prospectus supplement. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus supplement or in the documents incorporated by reference is accurate as of any date other than the date on the front of this prospectus supplement or those documents.

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein contain statements that are not historical facts and are considered forward-looking within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements, other than statements of historical facts, contained or incorporated by reference in this prospectus supplement 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”, “will”, “would” or the negative of these words or other comparable terminology, although not all forward-looking statements contain these identifying words. Forward-looking statements include, but are not limited to, statements about:

- our expectations related to the use of any net proceeds from this offering;
- the timing or likelihood of regulatory actions, filings and approvals for our current and future drug candidates, including our ability to obtain marketing approval for avapritinib and pralsetinib for additional indications or in additional geographies;
- our ability and plans in continuing to build out our commercial infrastructure and successfully launching, marketing and selling AYWAKIT (avapritinib) (marketed in Europe under the brand name AYWAKYT), GAVRETO (pralsetinib) and any current and future drug candidates for which we receive marketing approval;
- the rate and degree of market acceptance of AYWAKIT/AYWAKYT, GAVRETO and any current and future drug candidates for which we receive marketing approval;
- the pricing and reimbursement of AYWAKIT/AYWAKYT, GAVRETO and any current and future drug candidates for which we receive marketing approval;
- the initiation, timing, progress and results of our preclinical studies and clinical trials, including our ongoing clinical trials and any planned clinical trials for our current and future drug candidates and research and development programs;
- our ability to advance drug candidates into, and successfully complete, clinical trials;
- our ability to successfully develop manufacturing processes for any of our current and future drugs or drug candidates and to secure manufacturing, packaging and labeling arrangements for development activities and commercial production;
- the implementation of our business model and strategic plans for our business, drugs, drug candidates, platform and technology;
- the scope of protection we are able to establish and maintain for intellectual property rights covering our current and future drugs, drug candidates and technology;
- the potential benefits of our collaboration with F. Hoffmann-La Roche Ltd and Genentech, Inc. to develop and commercialize pralsetinib globally (excluding Greater China), our cancer immunotherapy collaboration with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., our collaboration with CStone Pharmaceuticals to develop and commercialize avapritinib, pralsetinib and fisogatinib in Greater China, and our collaboration with Zai Lab to develop and commercialize BLU-701 and BLU-945 as inhibitors of epidermal growth factor receptor (EGFR), as well as our ability to maintain these collaborations and establish additional strategic collaborations;
- the potential benefits of our exclusive license agreement with Clementia Pharmaceuticals, Inc. to develop and commercialize BLU-782 for fibrodysplasia ossificans progressive;
- the development of companion diagnostic tests for our current or future drugs or drug candidates;
- our financial performance, estimates of our revenues, expenses and capital requirements and our needs for future financing, including our ability to achieve a self-sustainable financial profile;
- developments relating to our competitors and our industry;

- the actual or potential benefits of designations granted by the U.S. Food and Drug Administration, or FDA, such as orphan drug, fast track and breakthrough therapy designation or priority review; and
- the impact and scope of the ongoing COVID-19 pandemic on our business, operations, strategy, goals and anticipated milestones, including our ongoing and planned research and discovery activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, and the launch, marketing, sale and commercial supply of AYYAKIT/AYVAKYT, GAVRETO and any current or future drug candidates for which we receive marketing approval.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, particularly in the “Risk Factors” section beginning on page [S-9](#) of this prospectus supplement and on page 49 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, as filed with the SEC on February 17, 2022, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into.

You should read this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, as well as the documents that we have filed as exhibits to the registration statement of which this prospectus supplement forms a part, completely and with the understanding that our actual future results, performance or achievements may be materially different from what we expect. 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.

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein also contain estimates, projections and other information concerning our industry, our business and the markets for certain diseases, including data regarding the estimated size of those markets, and the incidence and prevalence of certain medical conditions. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement, including the information incorporated by reference in this prospectus supplement, and the information included in the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering, including the information under the heading “Risk Factors” in this prospectus supplement on page [S-9](#) and in the documents incorporated by reference into this prospectus supplement.

Overview

We are a global precision therapy company that is inventing life-changing medicines for people with cancer and blood disorders. Applying an approach that is both precise and agile, we create therapies that selectively target genetic drivers, with the goal of staying one step ahead across stages of disease. Since 2011, we have leveraged our research platform, including expertise in molecular targeting and world-class drug design capabilities, to rapidly and reproducibly translate science into a broad pipeline of precision therapies. Today, we are delivering our approved medicines, AYVAKIT[®]/AYVAKYT[®] (avapritinib) and GAVRETO[®] (pralsetinib), to patients in the U.S. and Europe, and we are globally advancing multiple programs for systemic mastocytosis, or SM, lung cancer and other genomically defined cancers, and cancer immunotherapy.

Our drug discovery approach combines our biological insights with our proprietary compound library and chemistry expertise to design highly selective and potent precision therapies, with the goal of delivering significant and durable clinical benefit to patients based on the genetic driver of their disease. This uniquely targeted, scalable approach is designed to empower the rapid design and development of new treatments and increase the likelihood of success. In addition, our business model integrates our research engine with robust clinical development and commercial capabilities in oncology and hematology to create a cycle of innovation.

Our Strategy

Our vision is to leverage our scientific platform to design innovative first-in-class or best-in-class medicines targeting novel kinase biology and become a leading platform-enabled, fully-integrated, global precision therapy company focused on discovering, developing and commercializing a portfolio of precision therapies to patients with cancer and rare diseases.

Company Information

We were incorporated in Delaware in October 2008. Our mailing address and executive offices are located at 45 Sidney Street, Cambridge, Massachusetts 02139, and our telephone number is (617) 374-7580. We maintain an Internet website at the following address: www.blueprintmedicines.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. Our common stock trades on the Nasdaq Global Select Market under the symbol “BPMC”.

The trademarks, trade names and services marks appearing in this prospectus supplement and the accompanying prospectus are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus supplement may be referred to without the [®] and [™] symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

THE OFFERING	
Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$300.0 million
Common stock to be outstanding following this offering	Up to 62,746,421 shares (as more fully described in the notes following this table), assuming sales of 3,605,335 shares of our common stock in this offering at an offering price of \$83.21 per share, which was the last reported sale price of our common stock on the Nasdaq Global Select Market on February 15, 2022. The actual number of shares issued will vary depending on the sales price under this offering.
Manner of offering	“At the market offering” that may be made from time to time on the Nasdaq Global Select Market or other existing trading market for our common stock through our sales agent, Cowen. See “Plan of Distribution” on page S-15 of this prospectus supplement.
Use of proceeds	We intend to use the net proceeds from the sale of securities offered under this prospectus supplement primarily for general corporate purposes, which may include working capital and capital expenditures, expenses related to research, clinical development and commercial efforts, general and administrative expenses, and potential acquisitions of, or investments in, companies, technologies, products or assets that complement our business. See “Use of Proceeds” on page S-12 of this prospectus supplement for additional information.
Risk factors	Investing in our common stock involves risks. See “Risk Factors” beginning on page S-9 of this prospectus supplement and other information included or incorporated by reference into this prospectus supplement and the accompanying prospectus for a discussion of the factors you should carefully consider before deciding to invest in our securities.
Nasdaq Global Select Market symbol	“BPMC”
<p>The number of shares of common stock shown above to be outstanding after this offering is based on 59,141,086 shares outstanding as of December 31, 2021, and excludes as of that date:</p> <ul style="list-style-type: none"> • 5,682,022 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2021, at a weighted average exercise price of \$69.37 per share; • 1,590,160 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of December 31, 2021; • 3,027,882 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan, as of December 31, 2021, plus any future increases in the number of shares of common stock reserved for issuance under the 2015 Plan pursuant to the evergreen provision of the 2015 Plan; • 288,982 shares of common stock reserved for future issuance under our 2020 Inducement Plan as of December 31, 2021; and • 2,637,050 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan as of December 31, 2021. 	

In addition, unless we specifically state otherwise, all information in this prospectus supplement assumes:

- no exercise of outstanding stock options after December 31, 2021; and
- no vesting of restricted stock units after December 31, 2021.

RISK FACTORS

Investing in our common stock involves significant risks. In addition to the other information contained in this prospectus supplement, the accompanying prospectus and in the documents that we have incorporated by reference, you should carefully consider the risks discussed below and under the heading “Risk Factors” in our Annual Report on Form 10-K for the fiscal year ended December 31, 2021, filed with the SEC on February 17, 2022, as updated by our subsequent filings under the Exchange Act, before making a decision about investing in our common stock. Such risks and uncertainties and those discussed below are not the only ones facing us. Additional risks and uncertainties not presently known to us, or that we currently see as immaterial, may also harm our business. If any of these risks occur, our business, financial condition and operating results could be harmed, the trading price of our common stock could decline and you could lose part or all of your investment.

Risks Related to Our Common Stock and this Offering

The price of our common stock historically has been and may in the future be volatile and fluctuate substantially, which may affect the price at which you could sell the common stock.

Our stock price has been, and in the future may be, subject to substantial volatility. In addition, the stock market in general, and Nasdaq-listed and biopharmaceutical companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. For example, our stock traded within a range of a high price of \$117.86 per share on November 10, 2021 and a low price of \$66.29 per share on January 24, 2022 in the twelve-month period ending on February 16, 2022. As a result of this volatility, our stockholders could incur substantial losses. In addition, the market price for our common stock may be influenced by many factors, including:

- the success of competitive drugs or technologies;
- results of clinical trials of our drug candidates or those of our competitors;
- regulatory or legal developments in the U.S. and other countries;
- developments or disputes concerning patent applications, issued patents or other proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to any of our drug candidates or clinical development programs;
- the results of our efforts to discover, develop, acquire or in-license additional drug candidates or drugs;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions; and
- other risks and uncertainties described in these risk factors.

These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

We have broad discretion in how we use the proceeds of this offering, as well as our existing cash, cash equivalents and investments, and may not use them effectively, which could affect our results of operations and cause our stock price to decline.

We will have considerable discretion in the application of the net proceeds of this offering, including for any of the purposes described in the section entitled “Use of Proceeds,” as well as our existing cash, cash equivalents and investments, and you will be relying on the judgment of our management regarding such application. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. As a result, investors will be relying upon management’s judgment with only limited information about our specific intentions for the use of the balance of the net proceeds of this offering. We may use the net proceeds for purposes that do not yield a significant return or any return at all for our stockholders. In addition, pending their use, we may invest the net proceeds from this offering in a manner that does not produce income or that loses value.

Our executive officers, directors, principal stockholders and their affiliates maintain the ability to exercise significant influence over our company and all matters submitted to stockholders for approval.

Our executive officers, directors and stockholders who own more than 5% of our outstanding common stock, together with their affiliates and related persons, beneficially own shares of common stock representing a significant percentage of our capital stock. As a result, if these stockholders were to choose to act together, they would be able to influence our management and affairs and the outcome of matters submitted to our stockholders for approval, including the election of directors and any sale, merger, consolidation, or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

In addition, this concentration of ownership might adversely affect the market price of our common stock by:

- delaying, deferring or preventing a change of control of us;
- impeding a merger, consolidation, takeover or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

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

The offering price per share in this offering may exceed the as adjusted net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 3,605,335 shares of our common stock are sold at a price of \$83.21 per share, the last reported sale price of our common stock on the Nasdaq Global Select Market on February 15, 2022, for aggregate gross proceeds of \$300.0 million, and after deducting commissions and estimated offering expenses payable by us, you will experience immediate dilution of \$63.06 per share based on the difference between our as adjusted net tangible book value per share as of December 31, 2021 after giving effect to this offering and the assumed offering price.

This dilution is due to the substantially lower price paid by some of our investors who purchased shares prior to this offering as compared to the assumed price offered to the public in this offering, and the exercise of stock options granted to our employees. In addition, as of December 31, 2021, options to purchase 5,682,022 shares of our common stock at a weighted average exercise price of \$69.37 per share were outstanding, and 1,590,160 shares of our common stock would become issuable upon the vesting and settlement of restricted stock units outstanding as of such date. Each restricted stock unit represents a contingent right to receive one share of our common stock. The exercise of any of these options and the vesting and settlement of any of these restricted stock units would result in additional dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the assumed purchase price paid in this offering, if anything, in the event of our liquidation. Further, because we may seek to raise additional capital to fund our future activities, we may in the future sell substantial amounts of common stock or securities convertible into or exchangeable for common stock.

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

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

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

In addition, the sale of substantial amounts of our common stock could adversely impact its price. As of December 31, 2021, 59,141,086 shares of our common stock were outstanding, excluding options to purchase 5,682,022 shares of our common stock, of which 3,499,094 were exercisable as of that date, and 1,590,160 shares of our common stock issuable upon the vesting and settlement of restricted stock units outstanding as of that date. The sale or the availability for sale of a large number of shares of our common stock in the public market could cause the price of our common stock to decline.

The actual number of shares we will issue under the Sales Agreement, at any one time or in total, is uncertain.

Subject to certain limitations in the Sales Agreement and compliance with applicable law, we have the discretion to deliver a placement notice to Cowen at any time throughout the term of the Sales Agreement. The number of shares that are sold by Cowen after delivering a placement notice will fluctuate based on the market price of the shares of common stock during the sales period and limits we set with Cowen. Because the price per share of each share sold will fluctuate based on the market price of our common stock during the sales period, it is not possible at this stage to predict the number of shares that will be ultimately issued.

The common stock offered hereby will be sold in “at the market offerings,” and investors who buy shares at different times will likely pay different prices.

Investors who purchase shares in this offering at different times will likely pay different prices, and so may experience different outcomes in their investment results. We will have discretion, subject to market demand, to vary the timing, prices, and numbers of shares sold, and there is no minimum or maximum sales price. Investors may experience a decline in the value of their shares as a result of share sales made at prices lower than the prices they paid.

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 and economic conditions in the U.S. and abroad have contributed to the extreme volatility of the markets, which may have an effect on the market price of our common stock.

USE OF PROCEEDS

We may offer and sell shares of our common stock having aggregate gross sales proceeds of up to \$300,000,000 (before deducting sales agent commissions and expenses). Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time.

We anticipate that we will use the net proceeds to us from this offering to primarily for general corporate purposes, which may include working capital and capital expenditures, expenses related to research, clinical development and commercial efforts, general and administrative expenses, and potential acquisitions of, or investments in, companies, technologies, products or assets that complement our business.

This expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development efforts, the status of and results from non-clinical studies and ongoing clinical trials or any clinical trials we may commence in the future, the scope and results of our regulatory activities, the nature and scope of our commercial activities and future products, the success of our current or future collaborations, partnerships and license arrangements, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment-grade, interest-bearing instruments and U.S. government securities.

DILUTION

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

As of December 31, 2021, we had net tangible book value of approximately \$970.7 million, or \$16.41 per share of our common stock, based upon 59,141,086 shares of our common stock outstanding as of that date. Historical net tangible book value per share is equal to our total tangible assets, less total liabilities, divided by the number of outstanding shares of our common stock. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the assumed sale of 3,605,335 shares of common stock in this offering at an assumed offering price of \$83.21 per share, the last reported sale price of our common stock on the Nasdaq Global Select Market on February 15, 2022, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of December 31, 2021 would have been approximately \$1,264.5 million, or approximately \$20.15 per share of common stock. This represents an immediate increase in as adjusted net tangible book value of \$3.74 per share to our existing stockholders and an immediate dilution of \$63.06 per share to investors participating in this offering.

Dilution per share to new investors is determined by subtracting net tangible book value per share after this offering from the assumed offering price per share paid by new investors. The following table illustrates this per share dilution:

Assumed offering price per share	\$83.21
Historical net tangible book value per share as of December 31, 2021	\$16.41
Increase in net tangible book value per share attributable to new investors	\$ 3.74
As adjusted net tangible book value per share after this offering	\$20.15
Dilution per share to new investors	\$63.06

The as adjusted information is illustrative only and will adjust based on the actual offering price, the actual number of shares sold and other terms of the offering determined at the time shares of our common stock are sold pursuant to this prospectus supplement. The as adjusted information assumes that all of our common stock in the aggregate amount of \$300.0 million is sold at the assumed offering price of \$83.21 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on February 15, 2022. The shares sold in this offering, if any, will be sold from time to time at various prices.

The foregoing table and discussion is based on 59,141,086 shares of common stock outstanding as of December 31, 2021, and excludes:

- 5,682,022 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2021, at a weighted average exercise price of \$69.37 per share;
- 1,590,160 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of December 31, 2021;
- 3,027,882 shares of common stock reserved for future issuance under our 2015 Plan as of December 31, 2021;
- 288,982 shares of common stock reserved for future issuance under our 2020 Inducement Plan as of December 31, 2021; and
- 2,637,050 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan as of December 31, 2021.

The table above assumes for illustrative purposes that an aggregate of 3,605,335 shares of our common stock are sold during the term of the sales agreement with Cowen at a price of \$83.21 per share, the last

reported sale price of our common stock on the Nasdaq Global Select Market on February 15, 2022, for aggregate gross proceeds of approximately \$300.0 million.

To the extent that any options are vested and exercised or any restricted stock units are vested and settled, new options or restricted stock units 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.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Cowen, under which we may issue and sell from time to time up to \$300,000,000 of our common stock through or to Cowen as our sales agent or principal. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an “at the market offering” as defined in Rule 415 under the Securities Act.

Cowen will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party’s sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent equals up to 3.0% of the gross sales price of the shares sold through it pursuant to the sales agreement. We have also agreed to reimburse Cowen up to \$50,000 of Cowen’s actual outside legal expenses incurred by Cowen in connection with this offering. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$125,000.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on The Nasdaq Global Select Market on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the second business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

Under the sales agreement, we may also sell shares of common stock to Cowen as principal for its own account, at a price to be agreed upon at the time of sale. If we sell shares to a Cowen as principal, we will enter into a separate terms agreement with Cowen, and we will describe the agreement in a separate prospectus supplement or pricing supplement.

In connection with the sales of our common stock on our behalf, Cowen will be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to Cowen will be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilizes our common stock.

Our common stock is listed on The Nasdaq Global Select Market and trades under the symbol “BPMC.” The transfer agent of our common stock is Computershare Trust Company, N.A.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

LEGAL MATTERS

Certain legal matters in connection with this offering will be passed upon for us by Goodwin Procter LLP, Boston, Massachusetts. Cowen is being represented in this offering by Latham & Watkins LLP.

EXPERTS

The consolidated financial statements of Blueprint Medicines Corporation appearing in Blueprint Medicines Corporation's Annual Report on Form 10-K for the year ended December 31, 2021 and the effectiveness of Blueprint Medicines Corporation's internal control over financial reporting as of December 31, 2021 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of said firm as experts in auditing and accounting.

PROSPECTUS

Blueprint Medicines Corporation

Common Stock
Preferred Stock
Debt Securities
Purchase Contracts
Purchase Units
Warrants

We may offer and sell securities from time to time in one or more offerings. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in one or more supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement or amendment carefully before you invest in our securities.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on the Nasdaq Global Select Market under the symbol “BPMC.”

Investing in these securities involves significant risks. See “Risk Factors” included in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

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 February 13, 2020

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ABOUT THIS PROSPECTUS

This prospectus is part of an automatic registration statement that we filed with the Securities and Exchange Commission, which we refer to as the SEC, utilizing a “shelf” registration process as a “well-known seasoned issuer” as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings.

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading “Where You Can Find More Information” beginning on page 3 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in any accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

We use “AYVAKIT” and “Blueprint Medicines” as trademarks in the United States and other countries. This prospectus and the information incorporated herein by reference contains references to trademarks, service marks and trade names owned by us or other companies. Solely for convenience, trademarks, service marks and trade names referred to in this prospectus and the information incorporated herein, including logos, artwork, and other visual displays, may appear without the ® or ™ symbols, but such references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the rights of the applicable licensor to these trademarks, service marks and trade names. We do not intend our use or display of other companies’ trade names, service marks or trademarks to imply a relationship with, or endorsement or sponsorship of us by, any other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

Unless otherwise stated, all references in this prospectus, any applicable prospectus supplement and any related free writing prospectus to “us,” “our,” “Blueprint,” “Blueprint Medicines,” “we,” the “Company” and similar designations refer, collectively, to Blueprint Medicines Corporation, a Delaware corporation, and its consolidated subsidiaries.

RISK FACTORS

Investing in our securities involves significant risks. You should carefully consider the risks and uncertainties described in this prospectus and any accompanying prospectus supplement, including the risk factors set forth in our filings with the SEC that are incorporated by reference herein, including the risk factors in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, which is on file with the SEC and is incorporated herein by reference, and any of our subsequent filings with the SEC, before making an investment decision pursuant to this prospectus and any accompanying prospectus supplement relating to a specific offering.

Our business, financial condition and results of operations could be materially and adversely affected by any or all of these risks or by additional risks and uncertainties not presently known to us or that we currently deem immaterial that may adversely affect us in the future.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.blueprintmedicines.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiary and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's website.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-37359) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

- [Annual Report on Form 10-K for the fiscal year ended December 31, 2019, which was filed with the SEC on February 13, 2020;](#)
- The information specifically incorporated by reference into our [Annual Report on Form 10-K for the fiscal year ended December 31, 2018](#) from [our definitive proxy statement \(other than information furnished rather than filed\) for the 2019 Annual Meeting of Stockholders, which was filed with the SEC on April 29, 2019;](#) and
- The description of our common stock contained in our [Registration Statement on Form 8-A filed on April 27, 2015,](#) including any amendments or reports filed for the purpose of updating such description.

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

Blueprint Medicines Corporation
45 Sidney Street
Cambridge, Massachusetts 02139
Attn: Investor Relations
Phone: (617) 714-6674
E-mail: ir@blueprintmedicines.com

FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference in this prospectus include “forward-looking statements” within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements, other than statements of historical facts, contained or incorporated by reference in this prospectus are forward-looking statements. In some cases, you can identify forward-looking statements by words such as “aim,” “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “seek,” “should,” “target,” “will,” “would” or the negative of these words or other comparable terminology, although not all forward-looking statements contain these identifying words. Forward-looking statements include, but are not limited to, statements about the initiation, timing, progress and results of our pre-clinical studies and clinical trials, including our ongoing clinical trials and any planned clinical trials for avapritinib, pralsetinib, fisogatinib and BLU-263, and our research and development programs; our ability to advance drug candidates into, and successfully complete, clinical trials; the timing or likelihood of regulatory actions, filings and approvals for our drug candidates and our ability to successfully expand the indication for avapritinib, obtain marketing approval for avapritinib in additional jurisdictions and obtain marketing approval for pralsetinib; our ability and plans in continuing to build out our commercial infrastructure and successfully launching, marketing and selling AYWAKIT™ (avapritinib) and any future drug candidate for which we receive marketing approval in the U.S. and Europe; the rate and degree of market acceptance of AYWAKIT and any current and future drug candidates for which we receive marketing approval; the pricing and reimbursement of AYWAKIT and any future drugs for which we receive marketing approval; our ability to successfully develop manufacturing processes for our drug and drug candidates and secure manufacturing, packaging and labeling arrangements for development activities and commercial production; the implementation of our business model and strategic plans for our business, drug and drug candidates and technology; the scope of protection we are able to establish and maintain for intellectual property rights covering our drug, drug candidates and technology; the potential benefits of our collaborations with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. and CStone Pharmaceuticals, as well as our ability to maintain these collaborations and establish other strategic collaborations; the potential benefits of our exclusive license agreement with Clementia Pharmaceuticals, Inc.; the development of a companion diagnostic test for AYWAKIT to identify patients with a PDGFRA D842V mutation or companion diagnostic tests for our current or future drug candidates; our financial performance and estimates of our expenses, future revenues, capital requirements and our needs for future financing; and developments relating to our competitors and our industry.

Any forward-looking statements contained or incorporated by reference in this prospectus reflect our current views with respect to future events or to our future financial performance and 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 these forward-looking statements. See “Risk Factors” for more information. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make or enter into. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, whether as a result of new information, future events or otherwise.

BLUEPRINT MEDICINES CORPORATION

We are a precision therapy company focused on genomically defined cancers, rare diseases and cancer immunotherapy. Our approach is to leverage our novel target discovery engine to systematically and reproducibly identify kinases that are drivers of diseases and to craft highly selective and potent therapies that may provide significant and durable clinical responses for patients without adequate treatment options. This integrated biology and chemistry approach enables us to identify, characterize and design drug candidates to inhibit novel kinase targets that have been difficult to selectively inhibit. We believe that our uniquely targeted, scalable approach empowers the rapid design and development of new treatments and increases the likelihood of success.

We were incorporated in Delaware on October 14, 2008. Our mailing address and principal executive offices are located at 45 Sidney Street, Cambridge, Massachusetts 02139, and our telephone number is (617) 714-6674. We maintain an Internet website at the following address: www.blueprintmedicines.com. The information on, or that can be accessed through, our website does not constitute part of this prospectus, and you should not rely on any such information in making the decision whether to purchase our common stock. Our common stock trades on the Nasdaq Global Select Market under the symbol "BPMC."

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless the applicable prospectus supplement provides otherwise. General corporate purposes may include research and development costs of our drug candidates and to discover additional drug candidates, commercialization cost for any approved drugs, the acquisition or licensing of other drugs or drug candidates, business or technologies, working capital and capital expenditures. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including short-term, investment grade, interest bearing instruments and U.S. government securities, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DILUTION

If there is a material dilution of the purchasers' equity interest from the sale of common equity securities offered under this prospectus, we will set forth in any prospectus supplement the following information regarding any such material dilution of the equity interests of purchasers purchasing securities in an offering under this prospectus:

- the net tangible book value per share of our equity securities before and after the offering;
- the amount of the increase in such net tangible book value per share attributable to the cash payments made by the purchasers in the offering; and
- the amount of the immediate dilution from the public offering price which will be absorbed by such purchasers.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is intended as a summary only. This description is based upon, and is qualified by reference to, our amended and restated certificate of incorporation, or certificate of incorporation, our amended and restated bylaws, or bylaws, and applicable provisions of the Delaware General Corporation Law. This summary is not complete. You should read our certificate of incorporation and bylaws, which are filed as exhibits to the registration statement of which this prospectus forms a part, for the provisions that are important to you.

Common Stock

Annual Meeting. Annual meetings of our stockholders are held on the date designated in accordance with our bylaws. Written notice must be mailed to each stockholder entitled to vote not less than ten nor more than 60 days before the date of the meeting. The presence in person or by proxy of the holders of record of a majority of our issued and outstanding shares entitled to vote at such meeting constitutes a quorum for the transaction of business at meetings of the stockholders. Special meetings of the stockholders may be called for any purpose by the board of directors and shall be called by the chairman of the board or the secretary upon the written request, stating the purpose of such meeting, of the holders of a majority of the outstanding shares of all classes of capital stock entitled to vote at the meeting. Except as may be otherwise provided by applicable law, our certificate of incorporation or our bylaws, all elections shall be decided by a plurality, and all other questions shall be decided by a majority, of the votes cast by stockholders entitled to vote thereon at a duly held meeting of stockholders at which a quorum is present.

Voting Rights. Each holder of common stock is entitled to one vote for each share held on all matters to be voted upon by stockholders.

Dividends. The holders of common stock, after any preferences of holders of any preferred stock, are entitled to receive dividends when and if declared by the board of directors out of legally available funds.

Liquidation and Dissolution. If we are liquidated or dissolved, the holders of the common stock will be entitled to share in our assets available for distribution to stockholders in proportion to the amount of common stock they own. The amount available for common stockholders is calculated after payment of liabilities. Holders of any preferred stock will receive a preferential share of our assets before the holders of the common stock receive any assets.

Other Rights. Holders of the common stock have no right to convert the stock into any other security, have the stock redeemed or purchase additional stock or to maintain their proportionate ownership interest. The common stock does not have cumulative voting rights. Holders of shares of the common stock are not required to make additional capital contributions.

Nasdaq Global Select Market. Our common stock is listed on the Nasdaq Global Select Market under the trading symbol “BPMC.”

Transfer Agent and Registrar. Computershare Trust Company, N.A. is the transfer agent and registrar for our common stock.

Preferred Stock

We are authorized to issue “blank check” preferred stock, which may be issued in one or more series upon authorization of our board of directors. Our board of directors is authorized to fix the designation of the series, the number of authorized shares of the series, dividend rights and terms, conversion rights, voting rights, redemption rights and terms, liquidation preferences and any other rights, powers, preferences and limitations applicable to each series of preferred stock. The authorized shares of our preferred stock are available for issuance without further action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange on which our securities may be listed. If the approval of our stockholders is not required for the issuance of shares of our preferred stock, our board may determine not to seek stockholder approval. The specific terms of any series of preferred stock offered pursuant to this prospectus will be described in the prospectus supplement relating to that series of preferred stock.

A series of our preferred stock could, depending on the terms of such series, impede the completion of a merger, tender offer or other takeover attempt. Our board of directors will make any determination to issue shares of preferred stock based upon its judgment as to the best interests of our stockholders. Our board of directors, in so acting, could issue preferred stock having terms that could discourage an acquisition attempt through which an acquirer may be able to change the composition of our board of directors, including a tender offer or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over the then-current market price of the stock.

The preferred stock has the terms described below unless otherwise provided in the prospectus supplement relating to a particular series of preferred stock. You should read the prospectus supplement relating to the particular series of preferred stock being offered for specific terms, including:

- the designation and stated value per share of the preferred stock and the number of shares offered;
- the amount of liquidation preference per share;
- the price at which the preferred stock will be issued;
- the dividend rate, or method of calculation of dividends, the dates on which dividends will be payable, whether dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends will commence to accumulate;
- any redemption or sinking fund provisions;
- if other than the currency of the United States, the currency or currencies including composite currencies in which the preferred stock is denominated and/or in which payments will or may be payable;
- any conversion provisions; and
- any other rights, preferences, privileges, limitations and restrictions on the preferred stock.

The preferred stock will, when issued, be fully paid and nonassessable. Unless otherwise provided in the applicable prospectus supplement, each series of preferred stock will rank equally as to dividends and liquidation rights in all respects with each other series of preferred stock. The rights of holders of shares of each series of preferred stock will be subordinate to those of our general creditors.

Rank. Unless otherwise provided in the applicable prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon our liquidation, dissolution or winding up of our affairs, rank:

- senior to our common stock and to all equity securities ranking junior to such preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs;
- on a parity with all equity securities issued by us, the terms of which specifically provide that such equity securities rank on a parity with the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs; and
- junior to all equity securities issued by us, the terms of which specifically provide that such equity securities rank senior to the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs.

The term “equity securities” does not include convertible debt securities.

Dividends. Holders of the preferred stock of each series will be entitled to receive, when, as and if declared by our board of directors, cash dividends at such rates and on such dates described in the prospectus supplement. Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

Dividends on any series of preferred stock may be cumulative or noncumulative, as described in the applicable prospectus supplement. If our board of directors does not declare a dividend payable on a

dividend payment date on any series of noncumulative preferred stock, then the holders of that noncumulative preferred stock will have no right to receive a dividend for that dividend payment date, and we will have no obligation to pay the dividend accrued for that period, whether or not dividends on that series are declared payable on any future dividend payment dates. Dividends on any series of cumulative preferred stock will accrue from the date we initially issue shares of such series or such other date specified in the applicable prospectus supplement.

No dividends may be declared or paid or funds set apart for the payment of any dividends on any parity securities unless full dividends have been paid or set apart for payment on the preferred stock. If full dividends are not paid, the preferred stock will share dividends pro rata with the parity securities.

No dividends may be declared or paid or funds set apart for the payment of dividends on any junior securities unless full dividends for all dividend periods terminating on or prior to the date of the declaration or payment will have been paid or declared and a sum sufficient for the payment set apart for payment on the preferred stock.

Liquidation Preference. Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, then, before we make any distribution or payment to the holders of any common stock or any other class or series of our capital stock ranking junior to the preferred stock in the distribution of assets upon any liquidation, dissolution or winding up of our affairs, the holders of each series of preferred stock shall be entitled to receive out of assets legally available for distribution to stockholders, liquidating distributions in the amount of the liquidation preference per share set forth in the prospectus supplement, plus any accrued and unpaid dividends thereon. Such dividends will not include any accumulation in respect of unpaid noncumulative dividends for prior dividend periods. Unless otherwise provided in the applicable prospectus supplement, after payment of the full amount of their liquidating distributions, the holders of preferred stock will have no right or claim to any of our remaining assets. Upon any such voluntary or involuntary liquidation, dissolution or winding up, if our available assets are insufficient to pay the amount of the liquidating distributions on all outstanding preferred stock and the corresponding amounts payable on all other classes or series of our capital stock ranking on parity with the preferred stock and all other such classes or series of shares of capital stock ranking on parity with the preferred stock in the distribution of assets, then the holders of the preferred stock and all other such classes or series of capital stock will share ratably in any such distribution of assets in proportion to the full liquidating distributions to which they would otherwise be entitled.

Upon any such liquidation, dissolution or winding up and if we have made liquidating distributions in full to all holders of preferred stock, we will distribute our remaining assets among the holders of any other classes or series of capital stock ranking junior to the preferred stock according to their respective rights and preferences and, in each case, according to their respective number of shares. For such purposes, our consolidation or merger with or into any other corporation, trust or entity, or the sale, lease or conveyance of all or substantially all of our property or assets will not be deemed to constitute a liquidation, dissolution or winding up of our affairs.

Redemption. If so provided in the applicable prospectus supplement, the preferred stock will be subject to mandatory redemption or redemption at our option, as a whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in such prospectus supplement.

The prospectus supplement relating to a series of preferred stock that is subject to mandatory redemption will specify the number of shares of preferred stock that shall be redeemed by us in each year commencing after a date to be specified, at a redemption price per share to be specified, together with an amount equal to all accrued and unpaid dividends thereon to the date of redemption. Unless the shares have a cumulative dividend, such accrued dividends will not include any accumulation in respect of unpaid dividends for prior dividend periods. We may pay the redemption price in cash or other property, as specified in the applicable prospectus supplement. If the redemption price for preferred stock of any series is payable only from the net proceeds of the issuance of shares of our capital stock, the terms of such preferred stock may provide that, if no such shares of our capital stock shall have been issued or to the extent the net proceeds from any issuance are insufficient to pay in full the aggregate redemption price then due, such preferred stock shall automatically and mandatorily be converted into the applicable shares of our capital

stock pursuant to conversion provisions specified in the applicable prospectus supplement. Notwithstanding the foregoing, we will not redeem any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on the preferred stock for all past dividend periods and the then current dividend period; or
- if such series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends for the then current dividend period.

In addition, we will not acquire any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on all outstanding shares of such series of preferred stock for all past dividend periods and the then current dividend period; or
- if that series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends on the preferred stock of such series for the then current dividend period.

However, at any time we may purchase or acquire preferred stock of that series (1) pursuant to a purchase or exchange offer made on the same terms to holders of all outstanding preferred stock of such series or (2) by conversion into or exchange for shares of our capital stock ranking junior to the preferred stock of such series as to dividends and upon liquidation.

If fewer than all of the outstanding shares of preferred stock of any series are to be redeemed, we will determine the number of shares that may be redeemed pro rata from the holders of record of such shares in proportion to the number of such shares held or for which redemption is requested by such holder or by any other equitable manner that we determine. Such determination will reflect adjustments to avoid redemption of fractional shares.

Unless otherwise provided in the applicable prospectus supplement, we will mail notice of redemption at least 30 days but not more than 60 days before the redemption date to each holder of record of preferred stock to be redeemed at the address shown on our stock transfer books. Each notice shall state:

- the redemption date;
- the number of shares and series of preferred stock to be redeemed;
- the redemption price;
- the place or places where certificates for such preferred stock are to be surrendered for payment of the redemption price;
- that dividends on the shares to be redeemed will cease to accrue on such redemption date;
- the date on which the holder's conversion rights, if any, as to such shares shall terminate; and
- the specific number of shares to be redeemed from each such holder if fewer than all the shares of any series are to be redeemed.

If notice of redemption has been given and we have set aside the funds necessary for such redemption in trust for the benefit of the holders of any shares called for redemption, then from and after the redemption date, dividends will cease to accrue on such shares, and all rights of the holders of such shares will terminate, except the right to receive the redemption price.

Voting Rights. Holders of preferred stock will not have any voting rights, except as required by law or as indicated in the applicable prospectus supplement.

Unless otherwise provided for under the terms of any series of preferred stock, no consent or vote of the holders of shares of preferred stock or any series thereof shall be required for any amendment to our certificate of incorporation that would increase the number of authorized shares of preferred stock or the

number of authorized shares of any series thereof or decrease the number of authorized shares of preferred stock or the number of authorized shares of any series thereof (but not below the number of authorized shares of preferred stock or such series, as the case may be, then outstanding).

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into our common stock will be set forth in the applicable prospectus supplement relating thereto. Such terms will include the number of shares of common stock into which the shares of preferred stock are convertible, the conversion price, rate or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or at the option of the holders of the preferred stock, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption.

Transfer Agent and Registrar. The transfer agent and registrar for the preferred stock will be set forth in the applicable prospectus supplement.

Effects of Authorized but Unissued Stock

We have shares of common stock and preferred stock available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of the Nasdaq Global Select Market. We may utilize these additional shares for a variety of corporate purposes, including for future public offerings to raise additional capital or facilitate corporate acquisitions or for payment as a dividend on our capital stock. The existence of unissued and unreserved common stock and preferred stock may enable our board of directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a controlling interest in our company by means of a merger, tender offer, proxy contest or otherwise. In addition, if we issue preferred stock, the issuance could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation.

Registration Rights

We entered into a second amended and restated investors' rights agreement, dated as of November 7, 2014, which we refer to as the Investors' Rights Agreement, with the holders of shares of our common stock. Under the Investors' Rights Agreement, holders of registrable shares can demand that we file a registration statement or request that their shares be included on a registration statement that we are otherwise filing, in either case, registering the resale of their shares of common stock. These registration rights are subject to conditions and limitations, including the right, in certain circumstances, of the underwriters of an offering to limit the number of shares included in such registration and our right, in certain circumstances, not to effect a requested registration on Form S-1 within 60 days before or 180 days following any offering of our securities or a requested registration on Form S-3 within 30 days before or 90 days following any offering of our securities. The registration rights will terminate upon the earlier of the date on which all registrable shares have been sold and the date the registration rights terminate pursuant to the terms of the Investors' Rights Agreement.

Demand Registration Rights. The holders of at least a majority of our registrable shares may require us to file a registration statement under the Securities Act on a Form S-1 or Form S-3, if available, at our expense with respect to the resale of their registrable shares, and we are required to use our best efforts to effect the registration.

Piggyback Registration Rights. If we propose to register any of our securities under the Securities Act for our own account or the account of any other holder, the holders of registrable shares are entitled to notice of such registration and to request that we include registrable shares for resale on such registration statement, subject to the right of any underwriter to limit the number of shares included in such registration.

Expenses. We will pay all registration expenses, other than underwriting discounts and commissions, related to any demand or piggyback registration. The Investors' Rights Agreement contains customary cross-indemnification provisions pursuant to which we are obligated to indemnify the selling stockholders in the

event of misstatements or omissions in the registration statement attributable to us except in the event of fraud and they are obligated to indemnify us for misstatements or omissions attributable to them.

Provisions of our Certificate of Incorporation and Bylaws and Delaware Law That May Have Anti-takeover Effects

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

Board Composition and Filling Vacancies. In accordance with our certificate of incorporation, our board is divided into three classes serving three-year terms, with one class being elected each year. Our certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our board of directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office, even if less than a quorum.

No Written Consent of Stockholders. Our certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

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

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

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

Blank Check Preferred Stock. Our certificate of incorporation provides for 5,000,000 authorized shares of preferred stock. The existence of authorized but unissued shares of preferred stock may enable our board of directors to render more difficult or to discourage an attempt to obtain control of us by means

of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our board of directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our board of directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our board of directors broad power to establish the rights and preferences of authorized and unissued shares of preferred stock. The issuance of shares of preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us.

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

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

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

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

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to senior debt securities and subordinated debt securities collectively as debt securities. Each series of debt securities may have different terms. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series, under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information. As used in this prospectus, the term “debt securities” includes the debt securities being offered by this prospectus and all other debt securities issued by us under the indentures.

General

The indentures:

- do not limit the amount of debt securities that we may issue;
- allow us to issue debt securities in one or more series;
- do not require us to issue all of the debt securities of a series at the same time; and
- allow us to reopen a series to issue substantially identical additional debt securities without the consent of the holders of the debt securities of such series.

Unless otherwise provided in the applicable prospectus supplement, the senior debt securities will be unsubordinated obligations and will rank equally with all of our other unsecured and unsubordinated indebtedness. Payments on the subordinated debt securities will be subordinated to the prior payment in full of all of our senior indebtedness, as described under “— Subordination” and in the applicable prospectus supplement.

Each indenture provides that we may, but need not, designate more than one trustee under an indenture. Any trustee under an indenture may resign or be removed and a successor trustee may be appointed to act with respect to the series of debt securities administered by the resigning or removed trustee. If two or more persons are acting as trustee with respect to different series of debt securities, each trustee shall be a trustee of a trust under the applicable indenture separate and apart from the trust administered by any other trustee. Except as otherwise indicated in this prospectus, any action described in this prospectus to be taken by each trustee may be taken by each trustee with respect to, and only with respect to, the one or more series of debt securities for which it is trustee under the applicable indenture.

The prospectus supplement for each offering will provide the following terms, where applicable:

- the title of the debt securities and whether they are senior or subordinated;
- the aggregate principal amount of the debt securities being offered, the aggregate principal amount of the debt securities outstanding as of the most recent practicable date and any limit on their aggregate principal amount, including the aggregate principal amount of debt securities authorized;

- the price at which the debt securities will be issued, expressed as a percentage of the principal and, if other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof or, if applicable, the portion of the principal amount of such debt securities that is convertible into common stock or other securities of ours or the method by which any such portion shall be determined;
- if convertible, the terms on which such debt securities are convertible, including the initial conversion price or rate and the conversion period and any applicable limitations on the ownership or transferability of common stock or other securities of ours received on conversion;
- the date or dates, or the method for determining the date or dates, on which the principal of the debt securities will be payable;
- the fixed or variable interest rate or rates of the debt securities, or the method by which the interest rate or rates is determined;
- the date or dates, or the method for determining the date or dates, from which interest will accrue;
- the dates on which interest will be payable;
- the record dates for interest payment dates, or the method by which such dates will be determined;
- the persons to whom interest will be payable;
- the place or places where the principal of, and any premium or make-whole amount, and interest on, the debt securities will be payable;
- where the debt securities may be surrendered for registration of transfer or conversion or exchange;
- the times, prices and other terms and conditions upon which we may redeem the debt securities;
- any obligation we have to redeem, repay or repurchase the debt securities pursuant to any sinking fund or analogous provision or at the option of holders of the debt securities, and the times and prices at which we must redeem, repay or repurchase the debt securities as a result of such obligation;
- the currency or currencies in which the debt securities are denominated and payable if other than United States dollars, which may be a foreign currency or units of two or more foreign currencies or a composite currency or currencies and the terms and conditions relating thereto, and the manner of determining the equivalent of such foreign currency in United States dollars;
- whether the principal of, and any premium or make-whole amount, or interest on, the debt securities of the series are to be payable, at our election or at the election of a holder, in a currency or currencies other than that in which the debt securities are denominated or stated to be payable, and other related terms and conditions;
- whether the debt securities will be in registered form, bearer form, or both, and (i) if in registered form, the person to whom any interest shall be payable, if other than the person in whose name the security is registered at the close of business on the regular record date for such interest, or (ii) if in bearer form, the manner in which, or the person to whom, any interest on the security shall be payable if otherwise than upon presentation and surrender upon maturity;
- any restrictions applicable to the offer, sale or delivery of securities in bearer form and the terms upon which securities in bearer form of the series may be exchanged for securities in registered form of the series and vice versa, if permitted by applicable laws and regulations;
- whether any debt securities of the series are to be issuable initially in temporary global form and whether any debt securities of the series are to be issuable in permanent global form with or without coupons and, if so, whether beneficial owners of interests in any such permanent global security may, or shall be required to, exchange their interests for other debt securities of the series, and the manner in which interest shall be paid;
- the identity of the depositary for securities in registered form, if such series are to be issuable as a global security;
- the applicability, if any, of the defeasance and covenant defeasance provisions described in this prospectus or in the applicable indenture;

- whether and under what circumstances we will pay any additional amounts on the debt securities in respect of any tax, assessment or governmental charge;
- whether and under what circumstances the debt securities being offered are convertible into common stock or other securities of ours, as the case may be, including the conversion price or rate and the manner or calculation thereof;
- the name of the applicable trustee and the nature of any material relationship with us or any of our affiliates, and the percentage of debt securities of the class necessary to require the trustee to take action; and
- any other terms of such debt securities not inconsistent with the provisions of the applicable indenture.

We may issue debt securities that provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity of the debt securities. We refer to any such debt securities throughout this prospectus as “original issue discount securities.” The applicable prospectus supplement will describe the United States federal income tax consequences and other relevant considerations applicable to original issue discount securities.

Except as described under “— Merger, Consolidation or Sale of Assets” or as may be set forth in any prospectus supplement, the debt securities will not contain any provisions that (i) would limit our ability to incur indebtedness or (ii) would afford holders of debt securities protection in the event of (a) a highly leveraged or similar transaction involving us, or (b) a change of control or reorganization, restructuring, merger or similar transaction involving us that may adversely affect the holders of the debt securities. In the future, we may enter into transactions, such as the sale of all or substantially all of our assets or a merger or consolidation, that may have an adverse effect on our ability to service our indebtedness, including the debt securities, by, among other things, substantially reducing or eliminating our assets.

Our governing instruments do not define the term “substantially all” as it relates to the sale of assets. Additionally, Delaware cases interpreting the term “substantially all” rely upon the facts and circumstances of each particular case. Consequently, to determine whether a sale of “substantially all” of our assets has occurred, a holder of debt securities must review the financial and other information that we have disclosed to the public.

We will provide you with more information in the applicable prospectus supplement regarding any deletions, modifications, or additions to the events of default or covenants that are described below, including any addition of a covenant or other provision providing event risk or similar protection.

Payment

Unless otherwise provided in the applicable prospectus supplement, the principal of, and any premium or make-whole amount, and interest on, any series of the debt securities will be payable by mailing a check to the address of the person entitled to it as it appears in the applicable register for the debt securities or by wire transfer of funds to that person at an account maintained within the United States.

All monies that we pay to a paying agent or a trustee for the payment of the principal of, and any premium or make-whole amount, or interest on, any debt security will be repaid to us if unclaimed at the end of two years after the obligation underlying payment becomes due and payable. After funds have been returned to us, the holder of the debt security may look only to us for payment, without payment of interest for the period during which we hold the funds.

Denomination, Interest, Registration and Transfer

Unless otherwise provided in the applicable prospectus supplement, the debt securities of any series will be issuable in denominations of \$1,000 and integral multiples of \$1,000. Unless otherwise provided in the applicable prospectus supplement, interest on the debt securities shall be computed on the basis of a 360-day year composed of twelve 30-day months.

Subject to the limitations imposed upon debt securities that are evidenced by book entry in the records of a depository company rather than by physical delivery of a note, a holder of debt securities of any series may:

- exchange them for any authorized denomination of other debt securities of the same series and of a like aggregate principal amount and kind upon surrender of such debt securities at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose; and
- surrender them for registration of transfer or exchange at the corporate trust office of the applicable trustee or at the office of any transfer agent that we designate for such purpose.

Every debt security surrendered for registration of transfer or exchange must be accompanied by a written instrument of transfer satisfactory to the applicable trustee or transfer agent. Payment of a service charge will not be required for any registration of transfer or exchange of any debt securities, but we or the trustee may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection therewith. We may at any time designate additional transfer agents for any series of debt securities.

Neither we, nor any trustee, will be required to:

- issue, register the transfer of or exchange debt securities of any series during a period beginning at the opening of business 15 days before the day that the notice of redemption of any debt securities selected for redemption is mailed and ending at the close of business on the day of such mailing;
- register the transfer of or exchange any debt security, or portion thereof, so selected for redemption, in whole or in part, except the unredeemed portion of any debt security being redeemed in part; and
- issue, register the transfer of or exchange any debt security that has been surrendered for repayment at the option of the holder, except the portion, if any, of such debt security not to be so repaid.

Merger, Consolidation or Sale of Assets

The indentures provide that we may, without the consent of the holders of any outstanding debt securities, (i) consolidate with, (ii) sell, lease or convey all or substantially all of our assets to, or (iii) merge with or into, any other entity provided that:

- either we are the continuing entity, or the successor entity, if other than us, assumes the obligations (a) to pay the principal of, and any premium or make-whole amount, and interest on, all of the debt securities and (b) to duly perform and observe all of the covenants and conditions contained in the applicable indenture;
- after giving effect to the transaction, there is no event of default under the applicable indentures and no event which, after notice or the lapse of time, or both, would become such an event of default, occurs and continues; and
- an officers' certificate and legal opinion covering such conditions are delivered to each applicable trustee.

Events of Default, Notice and Waiver

Unless the applicable prospectus supplement states otherwise, when we refer to "events of default" as defined in the indentures with respect to any series of debt securities, we mean:

- default in the payment of any installment of interest on any debt security of such series continuing for 90 days unless such date has been extended or deferred;
- default in the payment of principal of, or any premium or make-whole amount on, any debt security of such series when due and payable unless such date has been extended or deferred;
- default in the performance or breach of any covenant or warranty in the debt securities or in the indenture by us continuing for 90 days after written notice described below;

- bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of us; and
- any other event of default provided with respect to a particular series of debt securities.

If an event of default occurs and is continuing with respect to debt securities of any series outstanding, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the principal amount of all the debt securities of that series to be due and payable. If the debt securities of that series are original issue discount securities or indexed securities, then the applicable trustee or the holders of 25% or more in principal amount of the debt securities of that series will have the right to declare the portion of the principal amount as may be specified in the terms thereof to be due and payable. However, at any time after such a declaration of acceleration has been made, but before a judgment or decree for payment of the money due has been obtained by the applicable trustee, the holders of at least a majority in principal amount of outstanding debt securities of such series or of all debt securities then outstanding under the applicable indenture may rescind and annul such declaration and its consequences if:

- we have deposited with the applicable trustee all required payments of the principal, any premium or make-whole amount, interest and, to the extent permitted by law, interest on overdue installment of interest, plus applicable fees, expenses, disbursements and advances of the applicable trustee; and
- all events of default, other than the non-payment of accelerated principal, or a specified portion thereof, and any premium or make-whole amount, have been cured or waived.

The indentures require each trustee to give notice to the holders of debt securities within the later of 90 days after an event of default and 30 days after the event of default is actually known to a responsible officer of such trustee, unless such default has been cured or waived. However, the trustee may withhold notice if specified persons of such trustee consider such withholding to be in the interest of the holders of debt securities.

The indentures provide that holders of debt securities of any series may not institute any proceedings, judicial or otherwise, with respect to such indenture or for any remedy under the indenture, unless the trustee fails to act for a period of 90 days after the trustee has received a written request to institute proceedings in respect of an event of default from the holders of 25% or more in principal amount of the outstanding debt securities of such series, as well as an offer of indemnity reasonably satisfactory to the trustee. However, this provision will not prevent any holder of debt securities from instituting suit for the enforcement of payment of the principal of, and any premium or make-whole amount, and interest on, such debt securities at the respective due dates thereof.

The indentures provide that, subject to provisions in each indenture relating to its duties in the case of a default, a trustee has no obligation to exercise any of its rights or powers at the request or direction of any holders of any series of debt securities then outstanding under the indenture, unless the holders have offered to the trustee reasonable security or indemnity. The holders of at least a majority in principal amount of the outstanding debt securities of any series or of all debt securities then outstanding under an indenture shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the applicable trustee, or of exercising any trust or power conferred upon such trustee. However, a trustee may refuse to follow any direction which:

- is in conflict with any law or the applicable indenture;
- may involve the trustee in personal liability; or
- may be unduly prejudicial to the holders of debt securities of the series not joining the proceeding.

Within 120 days after the close of each fiscal year, we will be required to deliver to each trustee a certificate, signed by one of our several specified officers, stating whether or not that officer has knowledge of any default under the applicable indenture. If the officer has knowledge of any default, the notice must specify the nature and status of the default.

Modification of the Indentures

The indentures provide that modifications and amendments may be made only with the consent of the affected holders of a majority in principal amount of all outstanding debt securities in that series issued under that indenture.

We and our respective trustee may make modifications and amendments of an indenture without the consent of any holder of debt securities for any of the following purposes:

- to evidence the succession of another person to us as obligor under such indenture;
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants for the benefit of the holders of all or any series of debt securities or to surrender any right or power conferred upon us in such indenture;
- to add events of default for the benefit of the holders of all or any series of debt securities;
- to add to, delete from, or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication, and delivery of debt securities;
- to make any change that does not adversely affect the rights of any securityholder in any material respect;
- to establish the form or terms of debt securities of any series;
- to provide for the acceptance of appointment by a successor trustee or facilitate the administration of the trusts under an indenture by more than one trustee; or
- to cure any ambiguity, defect or inconsistency in an indenture, provided that such action shall not adversely affect the interests of holders of debt securities of any series issued under such indenture.

Voting

The indentures provide that in determining whether the holders of the requisite principal amount of outstanding debt securities of a series have given any request, demand, authorization, direction, notice, consent or waiver under the indentures or whether a quorum is present at a meeting of holders of debt securities, the principal amount of an original issue discount security that shall be deemed to be outstanding shall be the amount of the principal thereof that would be due and payable as of the date of such determination upon declaration of acceleration of the maturity thereof.

Subordination

Unless otherwise provided in the applicable prospectus supplement, subordinated debt securities will be subject to the following subordination provisions.

Upon any distribution to our creditors in a liquidation, dissolution or reorganization, the payment of the principal of and interest on any subordinated debt securities will be subordinated to the extent provided in the applicable indenture in right of payment to the prior payment in full of all senior debt. However, our obligation to make payments of the principal of and interest on such subordinated debt securities otherwise will not be affected. No payment of principal or interest will be permitted to be made on subordinated debt securities at any time if a default on senior debt exists that permits the holders of such senior debt to accelerate its maturity and the default is the subject of judicial proceedings or we receive notice of the default. After all senior debt is paid in full and until the subordinated debt securities are paid in full, holders of subordinated debt securities will be subrogated to the rights of holders of senior debt to the extent that distributions otherwise payable to holders of subordinated debt securities have been applied to the payment of senior debt. The subordinated indenture will not restrict the amount of senior debt or other indebtedness of ours. As a result of these subordination provisions, in the event of a distribution of assets upon insolvency, holders of subordinated debt securities may recover less, ratably, than our general creditors.

No restrictions will be included in any indenture relating to subordinated debt securities upon the creation of additional senior debt.

If this prospectus is being delivered in connection with the offering of a series of subordinated debt securities, the accompanying prospectus supplement or the information incorporated in this prospectus by reference will set forth the approximate amount of senior debt outstanding as of the end of our most recent fiscal quarter.

Discharge, Defeasance and Covenant Defeasance

Unless otherwise provided in the applicable prospectus supplement, the indentures allow us to discharge our obligations to holders of any series of debt securities issued under any indenture when:

- either (i) all securities of such series have already been delivered to the applicable trustee for cancellation; or (ii) all securities of such series have not already been delivered to the applicable trustee for cancellation but (a) have become due and payable, (b) will become due and payable within one year, or (c) if redeemable at our option, are to be redeemed within one year, and we have irrevocably deposited with the applicable trustee, in trust, funds in such currency or currencies, currency unit or units or composite currency or currencies in which such debt securities are payable, an amount sufficient to pay the entire indebtedness on such debt securities
- in respect of principal and any premium or make-whole amount, and interest to the date of such deposit if such debt securities have become due and payable or, if they have not, to the stated maturity or redemption date;
- we have paid or caused to be paid all other sums payable; and
- an officers' certificate and an opinion of counsel stating the conditions to discharging the debt securities have been satisfied has been delivered to the trustee.

Unless otherwise provided in the applicable prospectus supplement, the indentures provide that, upon our irrevocable deposit with the applicable trustee, in trust, of an amount, in such currency or currencies, currency unit or units or composite currency or currencies in which such debt securities are payable at stated maturity, or government obligations, or both, applicable to such debt securities, which through the scheduled payment of principal and interest in accordance with their terms will provide money in an amount sufficient to pay the principal of, and any premium or make-whole amount, and interest on, such debt securities, and any mandatory sinking fund or analogous payments thereon, on the scheduled due dates therefor, the issuing company shall be released from its obligations with respect to such debt securities under the applicable indenture or, if provided in the applicable prospectus supplement, its obligations with respect to any other covenant, and any omission to comply with such obligations shall not constitute an event of default with respect to such debt securities.

Notwithstanding the above, we may not elect to defease and be discharged from the obligation to pay any additional amounts upon the occurrence of particular events of tax, assessment or governmental charge with respect to payments on such debt securities and the obligations to register the transfer or exchange of such debt securities, to replace temporary or mutilated, destroyed, lost or stolen debt securities, to maintain an office or agency in respect of such debt securities, or to hold monies for payment in trust.

The applicable prospectus supplement may further describe the provisions, if any, permitting such defeasance or covenant defeasance, including any modifications to the provisions described above, with respect to the debt securities of or within a particular series.

Conversion Rights

The terms and conditions, if any, upon which the debt securities are convertible into common stock or other securities of ours will be set forth in the applicable prospectus supplement. The terms will include whether the debt securities are convertible into shares of common stock or other securities of ours, the conversion price, or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at the issuing company's option or the option of the holders, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption of the debt securities and any restrictions on conversion.

No Recourse

No recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the debt securities, waives and releases all such liability.

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act is applicable.

DESCRIPTION OF PURCHASE CONTRACTS AND PURCHASE UNITS

We may issue purchase contracts, including contracts obligating holders to purchase from or sell to us, and obligating us to sell to or purchase from the holders, a specified number of shares of our common stock or preferred stock at a future date or dates, which we refer to in this prospectus as purchase contracts. The price per share of common stock or preferred stock and the number of shares of each may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula set forth in the purchase contracts. The purchase contracts may be issued separately or as part of units, often known as purchase units, consisting of one or more purchase contracts and beneficial interests in debt securities or any other securities described in the applicable prospectus supplement or any combination of the foregoing, securing the holders' obligations to purchase the common stock or preferred stock under the purchase contracts.

The purchase contracts may require us to make periodic payments to the holders of the purchase units or vice versa, and these payments may be unsecured or prefunded on some basis. The purchase contracts may require holders to secure their obligations under those contracts in a specified manner, including pledging their interest in another purchase contract.

The applicable prospectus supplement will describe the terms of the purchase contracts and purchase units, including, if applicable, collateral or depositary arrangements.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase debt securities, common stock or preferred stock. We may offer warrants separately or together with one or more additional warrants, debt securities, common stock or preferred stock, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the debt securities, common stock or preferred stock with which the warrants are issued and, the number of warrants issued with each security;
- if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, common stock or preferred stock will be separately transferable;
- the number of shares of common stock or the number of shares of preferred stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the antidilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;
- any redemption or call provisions; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

PLAN OF DISTRIBUTION

We may sell securities:

- to or through underwriters, brokers or dealers;
- through agents;
- directly to one or more other purchasers in negotiated sales or competitively bid transactions;
- in “at the market” offerings, within the meaning of Rule 415(a)(4) of the Securities Act of 1933, as amended, or the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise;
- through a block trade in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction; or
- through a combination of any of the above methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected from time to time in one or more transactions:

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

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- any discounts and commissions to be allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which the prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallocate in connection with the offering, creating a short position for their own accounts. In addition, to cover overallocations or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In compliance with the guidelines of the Financial Industry Regulatory Authority, or FINRA, the aggregate maximum discount, commission or agency fees or other items constituting underwriting compensation to be received by any FINRA member or independent broker-dealer will not exceed 8% of the proceeds from any offering pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Goodwin Procter LLP, Boston, Massachusetts.

EXPERTS

The consolidated financial statements of Blueprint Medicines Corporation appearing in Blueprint Medicines Corporation's Annual Report on Form 10-K for the year ended December 31, 2019 and the effectiveness of Blueprint Medicines Corporation's internal control over financial reporting as of December 31, 2019 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of said firm as experts in auditing and accounting.

Up to \$300,000,000



Common Stock

PROSPECTUS SUPPLEMENT

Cowen

February 17, 2022

Calculation of Filing Fee Table

424(b)(5)
(Form Type)

Blueprint Medicines Corporation
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered and Carry Forward Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price ⁽¹⁾	Fee Rate	Amount of Registration Fee ⁽²⁾	Carry Forward Form Type	Carry Forward File Number	Carry Forward Initial Effective Date	Filing Fee Previously Paid In Connection with Unsold Securities to be Carried Forward
Newly Registered Securities												
Fees to Be Paid	Equity	Common Stock, par value \$0.001 per share	Rule 457(r)	\$300,000,000		\$300,000,000	0.0000927	\$27,810				
Fees Previously Paid												
						\$300,000,000		\$27,810				
								\$ 0				
								\$27,810				

- (1) The proposed maximum aggregate offering price is being used to calculate the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.
- (2) Calculated in accordance with Rule 456(b) and Rule 457(r) of the Securities Act of 1933, as amended. This “Calculation of Registration Fee” table shall be deemed to update the “Calculation of Registration Fee” table in the registrant’s registration statement on Form S-3ASR filed with the Securities and Exchange Commission on February 13, 2020 (File No. 333-236424).