

Mirati Therapeutics, Inc.
Form 424B5
January 16, 2019
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**Filed Pursuant to Rule 424(b)(5)
Registration Statement No. 333-227209**

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

Subject to Completion, dated January 16, 2019

PRELIMINARY PROSPECTUS SUPPLEMENT

(To the Prospectus Dated September 6, 2018)

\$75,000,000

COMMON STOCK

PRE-FUNDED WARRANTS TO PURCHASE COMMON STOCK

We are offering \$75,000,000 of our common stock and, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase shares of common stock pursuant to this prospectus supplement and the accompanying prospectus. The purchase price of each pre-funded warrant will equal the price per share at which shares of common stock are being sold to the public in this offering, minus \$0.001, and the exercise price of each pre-funded warrant will equal \$0.001 per share. This prospectus supplement also relates to the offering of the shares of common stock issuable upon exercise of such pre-funded warrants.

Our common stock is listed on The Nasdaq Global Select Market under the symbol **MRTX**. The last reported sale price of our common stock on January 15, 2019 was \$64.80 per share. We do not intend to list the pre-funded

warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

An investment in our common stock involves a high degree of risk. Please read Risk Factors on page S-7 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement before investing in our securities.

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.

| | Per Share | Per Pre-Funded Warrant | Total |
|---|----------------------|---------------------------------------|--------------|
| Public offering price | \$ | \$ | \$ |
| Underwriting discounts and commissions ⁽¹⁾ | \$ | \$ | \$ |
| Proceeds, before expenses, to us | \$ | \$ | \$ |

(1) We refer you to Underwriting beginning on page S-15 of this prospectus supplement for information regarding underwriting compensation, including the reimbursement of certain of the underwriters' expenses.

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

The underwriters expect to deliver the shares against payment on or about January _____, 2019 through the book entry facilities of the Depository Trust Company. The pre-funded warrants are expected to be delivered on or about January _____, 2019.

J.P. Morgan

Citigroup

Cowen

Barclays

Credit Suisse

The date of this prospectus supplement is January _____, 2019.

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We have not, and the underwriters have not, authorized anyone to provide you with information different than that which is contained in or incorporated by reference in this prospectus supplement, the accompanying

prospectus and in any free writing prospectus that we have authorized for use in connection with this offering. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents

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incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled **Where You Can Find More Information and **Incorporation of Certain Information by Reference**.**

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated September 6, 2018, including the documents incorporated by reference therein, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or 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 in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement. You should assume that the information contained in this prospectus supplement is accurate as of the date on the front cover of this prospectus supplement only and that any information we have incorporated by reference or included in the accompanying prospectus is accurate only as of the date given in the document incorporated by reference or as of the date of the prospectus, as applicable, regardless of the time of delivery of this prospectus supplement or the accompanying prospectus or any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

Unless the context indicates otherwise, as used in this prospectus supplement, the terms Mirati, the Company, we, us, and our refer to Mirati Therapeutics, Inc., a Delaware corporation, and its subsidiaries on a consolidated basis.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference may include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus supplement or the accompanying prospectus are the property of their respective owners.

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PROSPECTUS SUPPLEMENT SUMMARY

*This summary highlights selected information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all the information you should consider before investing in our common stock. You should read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the factors described under the heading **Risk Factors** in this prospectus supplement and the financial and other information incorporated by reference in this prospectus supplement and the accompanying prospectus, as well as the information included in any free writing prospectus that we have authorized for use in connection with this offering, before making an investment decision.*

Our Company

We are a clinical-stage oncology company developing product candidates to address the genetic and immunological promoters of cancer. Our precision oncology clinical programs utilize genomic testing to identify and select cancer patients who we believe would be most likely to benefit from targeted drug treatment. In immuno-oncology, we are advancing our sitravatinib program which we believe has the potential to improve the immune environment of tumor cells and enhance and expand the efficacy of existing cancer immunotherapy medicines when given in combination. Our discovery programs include potentially first-in-class and best-in-class product candidates specifically designed to address mutations and tumors where few treatment options exist. We approach each of our discovery and development programs with a singular focus: to translate our deep understanding of the molecular drivers of cancer into better therapies and better outcomes for patients.

Our clinical pipeline consists of two product candidates: sitravatinib, a multi-kinase inhibitor and MRTX849, a KRAS G12C inhibitor. We maintain an active discovery program, including a preclinical program for a KRAS G12D inhibitor.

Sitravatinib in Combination with Immune Checkpoint Inhibitors

Sitravatinib is an investigational, spectrum-selective kinase inhibitor that is designed to potently inhibit receptor tyrosine kinases (RTKs), including TAM family receptors (TYRO3, Axl, Mer), split family receptors (VEGFR2, KIT) and RET. As an investigational immuno-oncology agent, sitravatinib is being evaluated in combination with nivolumab (OPDIVO®), Bristol Myers Squibb's anti-PD-1 checkpoint inhibitor, in a Phase 2 clinical trial in patients with non-small cell lung cancer (NSCLC) who have experienced documented disease progression following prior treatment with a checkpoint inhibitor. On October 22, 2018, we reported data from this ongoing clinical trial at the 2018 European Society of Medical Oncology Congress (ESMO), based on a data cutoff date of August 27, 2018. A summary of this data, with response confirmations updated after the data cutoff date, is presented below:

56 patients were evaluable for response with at least one radiographic scan. Patients had a median of two lines of previous therapy;

45 of 56 evaluable patients demonstrated tumor reductions; 18 of which demonstrated tumor reductions greater than 30%;

11 of 56 evaluable patients achieved a confirmed Partial Response (PR) or Complete Response;

26 of 56 evaluable patients remained on treatment at the time of data cut-off including eight responding patients;

A preliminary Kaplan-Meier estimate of median duration of response was greater than nine months, with six responding patients treated for more than six months and two responding patients treated for more than 12 months; and

The combination has shown an acceptable toxicity profile, and most adverse events reported by investigators were Grade 1 or 2.

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We held an end of Phase 2 meeting with the U.S. Food and Drug Administration (FDA) in the third quarter of 2018 with respect to the development of sitravatinib in combination with a checkpoint inhibitor in NSCLC. Based on feedback received from the FDA, we plan to initiate a Phase 3 randomized clinical trial in the first half of 2019 in second line NSCLC patients comparing the combination of sitravatinib plus nivolumab to docetaxel in patients whose tumors have progressed on prior checkpoint inhibitor therapy. The Phase 3 clinical trial will include an interim analysis of objective response rate as a surrogate endpoint to serve as the basis for a potential new drug application (NDA) submission seeking accelerated approval in the United States, which we expect to complete by the end of 2020, and the primary endpoint of the final analysis for the clinical trial will be overall survival, which we expect to complete by the end of 2021. Ultimately, we believe the results of this clinical trial will enable an NDA for the treatment of NSCLC patients whose tumors have progressed following treatment with a platinum-containing regimen and a checkpoint inhibitor.

In January 2019, we announced a clinical collaboration with Bristol-Myers Squibb Company (Bristol-Myers Squibb) in connection with this Phase 3 clinical trial. Under the terms of the collaboration, Mirati will sponsor and fund the clinical trial and Bristol-Myers Squibb will provide nivolumab at no cost. In certain specified cases, Bristol-Myers Squibb will have an exclusive right to negotiate a commercial agreement with us for a limited period of time with respect to developing and commercializing sitravatinib worldwide excluding certain territories in Asia, Australia and New Zealand. We maintain global development and commercial rights to sitravatinib outside of certain Asian territories, where we have partnered with BeiGene Ltd. (BeiGene), and we are free to develop the program in combination with other agents.

During the third quarter of 2018, we initiated an open label Phase 2 clinical trial of sitravatinib combined with nivolumab in patients with advanced or metastatic urothelial carcinoma who previously failed treatment with an immune checkpoint inhibitor. We expect to receive initial data from this study in the second half of 2019.

During the third quarter of 2018, we also initiated an open label Phase 2 window of opportunity clinical trial to assess the mechanism of action of sitravatinib combined with nivolumab in patients with advanced clear cell renal cell cancer (RCC). We expect to receive initial data from this trial in the first half of 2019.

Sitravatinib as a Single Agent

Sitravatinib is also being evaluated as a single agent in a Phase 1b expansion clinical trial in patients with NSCLC and other tumor types who have specific genetic alterations in CBL, CHR4Q12 and RET. On October 21, 2018, we reported data from this clinical trial in a presentation at ESMO. The presentation provided an update from the pre-planned expansion cohort of the Phase 1b clinical trial of single agent sitravatinib in patients with CBL inactivating mutations. As of the data cut-off on September 4, 2018, eight patients were evaluable:

In the subset of evaluable NSCLC patients (n=2), one confirmed PR was observed, and one patient experienced stable disease with notable tumor regression;

In the subset of evaluable melanoma patients (n=2), one confirmed PR was observed, and one patient had stable disease; and

In the subset of evaluable patients with other solid tumors (n=4), two had stable disease and two had progression of disease.

CBL mutations are present in 1.5% of NSCLC tumors, 3.5% of melanoma tumors, and 2% of cancers of unknown origin.

Enrollment continues in this Phase 1b expansion clinical trial with an emphasis on patients with CBL inactivating mutations in NSCLC and melanoma. We expect to provide a clinical update in the second half of 2019 and to define a potential registration pathway based on updated data at that time.

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Interim clinical data from the ongoing Phase 1b expansion clinical trial were also presented in a poster at the American Society of Clinical Oncology (ASCO) Annual Meeting held on June 1 5, 2018 in Chicago, Illinois. The presentation, titled Evaluation of the spectrum selective RTK inhibitor sitravatinib in RCC refractory to anti-angiogenic therapy reported data from patients with RCC treated with single agent sitravatinib. Confirmed partial responses were reported in 20% of patients (4 of 20) with advanced, metastatic RCC who were refractory to prior treatment.

Sitratavinib Development in Collaboration with BeiGene, Ltd.

In January 2018, we entered into a Collaboration and License Agreement (the BeiGene Agreement) with BeiGene, pursuant to which we and BeiGene agreed to collaboratively develop sitravatinib in Asia (excluding Japan and certain other countries), Australia and New Zealand (the Licensed Territory). Under the BeiGene Agreement, we granted BeiGene an exclusive license to develop, manufacture and commercialize sitravatinib in the Licensed Territory, and we retained exclusive rights for the development, manufacturing and commercialization of sitravatinib outside the Licensed Territory.

During the fourth quarter of 2018, BeiGene initiated clinical trials evaluating sitravatinib in combination with tislelizumab, BeiGene s clinical-stage PD-1 checkpoint inhibitor. BeiGene s clinical trials are evaluating the combination of sitravatinib and tislelizumab in patients with NSCLC, RCC, hepatocellular cancer, gastric cancer and ovarian cancer. We expect to receive initial proof of concept data from these trials in the second half of 2019 and the first half of 2020.

KRAS Inhibitor Program

Our KRAS inhibitor program is focused on the discovery and development of small molecule compounds that target KRAS G12C and G12D. Our lead G12C compound, MRTX849, is an investigational, specific, potent and orally available small molecule. MRTX849 is designed to inhibit a form of KRAS which harbors a G12C mutation. KRAS G12C mutations are present in approximately 14% of NSCLC adenocarcinoma patients and 5% of colorectal cancer (CRC) patients as well as a small percentage of other tumors (e.g. pancreatic). Tumors characterized by KRAS G12C mutations are commonly associated with poor prognosis and resistance to therapy, and patients with these mutations have few treatment options. Single agent treatment with MRTX849 has shown complete regression of a subset of KRAS G12C-positive human tumor models implanted in mice. We received FDA authorization of our Investigational New Drug Application for MRTX849 in November 2018, and on January 15, 2019, we announced that we had dosed the first patient in a Phase 1/2 trial in patients with advanced solid tumors that harbor G12C mutations. Following dose escalation, we plan to expand into cohorts that include patients with NSCLC, CRC and those with other tumors that carry the G12C mutation. We expect to report early clinical results in the second half of 2019.

We also intend to expand our KRAS inhibitor program to target G12D mutations and expect to identify a clinical candidate targeting G12D mutations by the fourth quarter of 2019.

Mocetinostat

Mocetinostat is an investigational, oral, Class 1 and IV selective histone deacetylase inhibitor that was evaluated in a Phase 2 clinical trial combining mocetinostat with durvalumab (IMFINZI®) in NSCLC patients who experienced documented disease progression following prior treatment with an immune checkpoint inhibitor. In November 2018, we reported our strategic portfolio decision to deprioritize mocetinostat. We plan to explore licensing opportunities for mocetinostat.

Financial Update

Based on our current estimates, as of December 31, 2018, we had \$222.8 million in cash, cash equivalents and short-term investments. This amount is preliminary, has not been audited and is subject to change upon completion of the audit of our consolidated financial statements as of and for the year ended December 31, 2018.

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Corporate Information

We were incorporated in Delaware in April 2013. Our principal executive offices are located at 9393 Towne Centre Drive, Suite 200, San Diego, California 92121, and our telephone number is (858) 332-3410. Our corporate website address is www.mirati.com. We do not incorporate by reference into this prospectus the information on, or accessible through, our website, and you should not consider it as part of this prospectus.

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The number of shares of our common stock to be outstanding immediately after this offering is based on 32,516,041 shares outstanding as of September 30, 2018 and excludes the shares of common stock issuable upon exercise of the pre-funded warrants being offered by us in this offering, as well as:

3,577,471 shares of common stock issuable upon the exercise of outstanding stock options under our equity incentive plans, with a weighted average exercise price of \$18.86 per share;

2,012,956 shares of common stock available for future grants under our 2013 equity incentive plan;

164,650 shares of common stock available for issuance under our 2013 employee stock purchase plan; and

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11,817,912 shares of common stock issuable upon the exercise of outstanding pre-funded warrants at an exercise price of \$0.001 per share.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase additional shares and no exercise of the pre-funded warrants we are offering to certain purchasers.

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RISK FACTORS

Investing in our common stock involves a high degree of risk. Our business, prospects, financial condition or operating results could be materially adversely affected by the risks identified below, as well as other risks not currently known to us or that we currently consider immaterial. The trading price of our common stock could decline due to any of these risks, and you may lose all or part of your investment. In assessing the risks described below, you should also refer to the information contained in our Annual Report on Form 10-K for the year ended December 31, 2017, in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2018 and in the other documents which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety.

Risks Related to this Offering

Management will have broad discretion as to the use of the net proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on our business, delay the development of our product candidates, and cause the price of our common stock to decline.

If you purchase the common stock sold in this offering, you will experience immediate and substantial dilution in your investment. You will experience further dilution if we issue additional equity securities in the future.

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution with respect to the net tangible book value of the common stock you purchase in this offering. Based on the public offering price of \$ per share and our net tangible book value as of September 30, 2018, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of \$ per share with respect to the net tangible book value of the common stock. See Dilution for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

In addition, we have a significant number of stock options and warrants outstanding. To the extent that outstanding stock options or warrants have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution. 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 or result in downward pressure on the price of our common stock.

There is no public market for the pre-funded warrants being offered in this offering.

There is no established public trading market for the pre-funded warrants being offered in this offering, and we do not expect a market to develop. In addition, we do not intend to apply to list the pre-funded warrants on any securities exchange or nationally recognized trading system, including the Nasdaq Global Select Market. Without an active market, the liquidity of the pre-funded warrants will be limited.

Holders of pre-funded warrants purchased in this offering will have no rights as common stockholders until such holders exercise their pre-funded warrants and acquire our common stock.

Until holders of pre-funded warrants acquire shares of our common stock upon exercise of the pre-funded warrants, holders of pre-funded warrants will have no rights with respect to the shares of our common stock underlying such pre-funded warrants. Upon exercise of the pre-funded warrants, the holders will be entitled to exercise the rights of a common stockholder only as to matters for which the record date occurs after the exercise date.

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FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, and the documents incorporated by reference herein and therein contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve a number of risks and uncertainties. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as believes, expects, hopes, may, will, plan, intends, estimates, could, should, would, continue, seeks, pro forma, or anticipated words (including their use in the negative), or by discussions of future matters such as the development of current or future product candidates, timing of potential development activities and milestones, business plans and strategies, possible changes in legislation and other statements that are not historical. These statements include but are not limited to statements under the captions Business, Risk Factors and Management's Discussion and Analysis of Financial Condition and Results of Operations and in other sections incorporated by reference from our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as applicable, as well as our other filings with the SEC. You should be aware that the occurrence of any of the events discussed under the heading Risk Factors in any applicable prospectus supplement and any documents incorporated by reference herein or therein could substantially harm our business, operating results and financial condition and that if any of these events occurs, it could adversely affect the value of an investment in our securities.

We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. Before deciding to purchase our common stock, you should carefully consider the risk factors incorporated by reference herein, in addition to the other information set forth in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein.

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Based upon the public offering price of \$ per share and \$ per pre-funded warrant, we estimate that we will receive net proceeds of approximately \$ million (or approximately \$ million if the underwriters' option to purchase additional shares is exercised in full) from the sale of the securities offered by us in this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for general corporate purposes, including expenses related to the clinical development of sitravatinib and MRTX849, the preclinical development of our KRAS G12D inhibitor and the development of other preclinical programs, and for working capital.

The amounts and timing of these expenditures will depend on a number of factors, such as the timing and progress of our research and development efforts, the timing and progress of any partnering efforts, and the competitive environment for our product candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses for the net proceeds to us from this offering. Accordingly, our management will have broad discretion in the application of these proceeds. Pending application of the net proceeds as described above, we intend to temporarily invest the proceeds in short term, interest-bearing instruments.

PRICE RANGE OF OUR COMMON STOCK

On January 15, 2019, the closing price for our common stock as reported on The Nasdaq Global Select Market was \$64.80 per share. The following table sets forth the ranges of high and low sales prices per share of our common stock as reported on The Nasdaq Global Select Market and The Nasdaq Capital Market, as applicable, for the periods indicated. Such quotations represent inter-dealer prices without retail markup, markdown or commission and may not necessarily represent actual transactions.

| | High | Low |
|--|-------------|------------|
| Year Ended December 31, 2017 | | |
| First Quarter | \$ 6.30 | \$ 4.75 |
| Second Quarter | \$ 5.25 | \$ 2.70 |
| Third Quarter | \$ 12.40 | \$ 3.10 |
| Fourth Quarter | \$ 19.70 | \$ 11.50 |
| Year Ended December 31, 2018 | | |
| First Quarter | \$ 37.62 | \$ 17.15 |
| Second Quarter | \$ 53.50 | \$ 26.00 |
| Third Quarter | \$ 65.35 | \$ 44.35 |
| Fourth Quarter | \$ 43.50 | \$ 34.39 |
| Year Ended December 31, 2019 | | |
| First Quarter (through January 15, 2019) | \$ 66.73 | \$ 40.91 |

As of September 30, 2018, there were 15 stockholders of record of our common stock, which excludes stockholders whose shares were held in nominee or street name by brokers. The actual number of common stockholders is greater than the number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees. This number of holders of record also does not include stockholders whose shares may be held in trust by other entities.

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DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

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Investors purchasing shares of our common stock in this offering will experience immediate and substantial dilution in the pro forma net tangible book value of their shares of common stock. Dilution in pro forma net tangible book value represents the difference between the public offering price per share and the pro forma net tangible book value per share of our common stock immediately after the offering.

The historical net tangible book value of our common stock as of September 30, 2018 was \$225.1 million, or \$6.92 per share. Historical net tangible book value per share of our common stock represents our total tangible assets (total assets less intangible assets) less total liabilities divided by the number of shares of common stock outstanding as of that date.

After giving effect to the issuance of _____ shares of common stock and pre-funded warrants to purchase up to _____ shares of our common stock in this offering at the public offering price of \$ _____ per share of our common stock and \$ _____ per pre-funded warrant (which equals the public offering price per share of the common stock less the \$0.001 per share exercise price of each such pre-funded warrant) (and excluding shares of common stock issued and any proceeds received upon exercise of the warrants or any resulting accounting associated with the warrants) and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and excluding the proceeds, if any, from the exercise of the pre-funded warrants issued pursuant to this offering, our as adjusted net tangible book value as of September 30, 2018 would have been approximately \$ _____ million, or \$ _____ per share of common stock. This represents an immediate increase in net tangible book value of \$ _____ per share to existing stockholders and an immediate dilution of \$ _____ per share to new investors purchasing our common stock and pre-funded warrants in this offering.

The following table illustrates this dilution on a per share basis to new investors:

| | |
|--|---------|
| Public offering price per share | \$ |
| Historical net tangible book value per share as of September 30, 2018 | \$ 6.92 |
| Increase in net tangible book value per share attributable to new investors purchasing shares and pre-funded warrants in this offering | |

As adjusted net tangible book value per share after giving effect to this offering

| | |
|--|----|
| Dilution per share to new investors participating in this offering | \$ |
|--|----|

Assuming the pre-funded warrants were immediately exercised, this would result in an as adjusted net tangible book value per share after giving effect to this offering and warrant exercise of \$ _____, which represents a dilution per share to new investors of \$ _____, and an increase in net tangible book value per share to existing shareholders of \$ _____.

The information discussed above is illustrative only and will adjust based on the actual public offering price, the actual number of shares and pre-funded warrants that we offer in this offering, and other terms of this offering determined at pricing.

If the underwriters exercise their option in full to purchase an additional _____ shares of common stock in this offering, the as adjusted net tangible book value per share after the offering would be \$ _____ per share, the increase in the net tangible book value per share to existing stockholders would be \$ _____ per share and the dilution to new

investors purchasing our common stock in this offering would be \$ per share.

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The above discussion and table are based on 32,516,041 shares of common stock outstanding as of September 30, 2018, which does not include the shares of common stock issuable upon exercise of the pre-funded warrants being offered by us in this offering or:

3,577,471 shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2018, at a weighted-average exercise price of \$18.86 per share;

2,012,956 shares of common stock reserved for future issuance under the 2013 Equity Incentive Plan as of September 30, 2018;

164,650 shares of common stock reserved for future issuance under the 2013 Employee Stock Purchase Plan as of September 30, 2018; and

11,817,912 shares of common stock issuable upon the exercise of outstanding pre-funded warrants at an exercise price of \$0.001 per share.

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 we raise additional capital by issuing equity securities or convertible debt, your ownership will be further diluted.

To the extent that new options are issued under our share-based compensation plans or we issue additional shares of common stock under the ESPP in the future, there will be further dilution to investors participating in this offering.

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DESCRIPTION OF PRE-FUNDED WARRANTS

The following is a brief summary of certain terms and conditions of the pre-funded warrants being offered by this prospectus supplement. The following description is subject in all respects to the provisions contained in the pre-funded warrants.

Form. The pre-funded warrants will be issued as individual warrant agreements to the investors. The form of pre-funded warrant will be filed as an exhibit to our Current Report on Form 8-K that we expect to file with the SEC on January 17, 2019.

Exercisability. The pre-funded warrants are exercisable at any time after their original issuance. The pre-funded warrants will be exercisable, at the option of each holder, in whole or in part by delivering to us a duly executed exercise notice and by payment in full in immediately available funds for the number of shares of common stock purchased upon such exercise. As an alternative to payment in immediately available funds, the holder may, in its sole discretion, elect to exercise the pre-funded warrant through a cashless exercise, in which case the holder would receive upon such exercise the net number of shares of common stock determined according to the formula set forth in the pre-funded warrant. No fractional shares of common stock will be issued in connection with the exercise of a pre-funded warrant. In lieu of fractional shares, we will pay the holder an amount in cash equal to the fractional amount multiplied by the fair market value of any such fractional shares.

Exercise Limitations. Under the pre-funded warrants, we may not effect the exercise of any pre-funded warrant, and a holder will not be entitled to exercise any portion of any pre-funded warrant, which, upon giving effect to such exercise, would cause (i) the aggregate number of shares of our common stock beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the number of shares of our common stock outstanding immediately after giving effect to the exercise, or (ii) the combined voting power of our securities beneficially owned by the holder (together with its affiliates) to exceed 9.99% of the combined voting power of all of our securities then outstanding immediately after giving effect to the exercise, as such percentage ownership is determined in accordance with the terms of the pre-funded warrants. However, any holder may increase or decrease such percentage to any other percentage not in excess of 9.99% upon at least 61 days' prior notice from the holder to us.

Exercise Price. The exercise price per whole share of our common stock purchasable upon the exercise of the pre-funded warrants is \$0.001 per share of common stock. The exercise price of the pre-funded warrants is subject to appropriate adjustment in the event of certain stock dividends and distributions, stock splits, stock combinations, reclassifications or similar events affecting our common stock and also upon any distributions of assets, including cash, stock or other property to our stockholders.

Transferability. Subject to applicable laws, the pre-funded warrants may be offered for sale, sold, transferred or assigned without our consent.

Exchange Listing. We do not plan on applying to list the pre-funded warrants on The Nasdaq Global Select Market, any other national securities exchange or any other nationally recognized trading system.

Fundamental Transactions. In the event of a fundamental transaction, as described in the pre-funded warrants and generally including any reorganization, recapitalization or reclassification of our common stock, the sale, transfer or other disposition of all or substantially all of our properties or assets, our consolidation or merger with or into another person, the acquisition of more than 50% of our outstanding common stock, or any person or group becoming the beneficial owner of 50% of the voting power represented by our outstanding common stock, the holders of the pre-funded warrants will be entitled to receive upon exercise of the pre-funded warrants the kind and amount of

securities, cash or other property that the holders would have received had they exercised the

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pre-funded warrants immediately prior to such fundamental transaction without regard to any limitations on exercised contained in the pre-funded warrants.

No Rights as a Stockholder. Except by virtue of such holder's ownership of shares of our common stock, the holder of a pre-funded warrant does not have the rights or privileges of a holder of our common stock, including any voting rights, until the holder exercises the pre-funded warrant.

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Table of Contents**UNDERWRITING**

We have entered into an underwriting agreement with J.P. Morgan Securities LLC, Citigroup Global Markets Inc., Cowen and Company, LLC, Barclays Capital Inc. and Credit Suisse Securities (USA) LLC as representatives of the several underwriters named below with respect to the common stock and pre-funded warrants being offered. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase from us the number of shares of our common stock or pre-funded warrants set forth opposite its name below.

| | Number of Shares | Number of Pre-Funded Warrants |
|------------------------------------|-----------------------------|--|
| J.P. Morgan Securities LLC | | |
| Citigroup Global Markets Inc. | | |
| Cowen and Company, LLC | | |
| Barclays Capital Inc. | | |
| | | |
| Credit Suisse Securities (USA) LLC | | |
| | | |
| Total | | |

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent and that the underwriters have agreed, severally and not jointly, to purchase all of the shares and pre-funded warrants sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the option described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

We have agreed to indemnify the underwriters against specified liabilities, including liabilities under the Securities Act, and to contribute to payments the underwriters may be required to make in respect thereof.

The underwriters are offering the shares and pre-funded warrants, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel and other conditions specified in the underwriting agreement. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Option to Purchase Additional Shares. We have granted to the underwriters an option to purchase up to additional shares of common stock at the public offering price, less the underwriting discounts and commissions. This option is exercisable for a period of 30 days. The number of shares subject to the underwriters option will equal 15% of the total number of shares of common stock we are offering plus the shares underlying the pre-funded warrants. To the extent that the underwriters exercise this option, the underwriters will purchase additional shares from us in approximately the same proportion as shown in the column Number of Shares in the table above.

Discounts and Commissions. The following table shows the public offering price, underwriting discounts and commissions and proceeds, before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters option to purchase additional shares.

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We estimate that the total expenses of the offering, excluding underwriting discount, will be approximately \$ and are payable by us. We also have agreed to reimburse the underwriters for certain of their expenses in an amount up to \$15,000.

| | Per Share | Per Pre-Funded Warrant | Total Without Over-Allotment | Total With Over Allotment |
|--------------------------------------|------------------|-------------------------------|-------------------------------------|----------------------------------|
| Public offering price | \$ | \$ | \$ | \$ |
| Underwriting discount | \$ | \$ | \$ | \$ |
| Proceeds, before expenses, to Mirati | \$ | \$ | \$ | \$ |

The underwriters propose to offer the shares of common stock and pre-funded warrants to the public at the public offering price set forth on the cover of this prospectus. The underwriters may offer the shares of common stock to securities dealers at the public offering price less a concession not in excess of \$ per share. If all of the shares are not sold at the public offering price, the underwriters may change the offering price and other selling terms.

Nasdaq Global Select Market Listing. Our common stock is listed on The Nasdaq Global Select Market under the symbol MRTX. The pre-funded warrants will not be listed on any national securities exchange.

Stabilization. In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters' option to purchase additional shares referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The Nasdaq Global Select Market, in the over the counter market or otherwise.

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Passive Market Making. In connection with this offering, underwriters and selling group members may engage in passive market making transactions in our common stock on the Nasdaq Stock Market in accordance with Rule 103 of Regulation M under the Exchange Act, as amended, during a period before the commencement of offers or sales of common stock and extending through the completion of the distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, such bid must then be lowered when specified purchase limits are exceeded.

Lock-Up Agreements. We and our executive officers and directors have agreed, with certain limited exceptions, not to sell, hedge or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 90 days after the date of this prospectus without first obtaining the written consent of J.P. Morgan Securities LLC and Citigroup Global Markets Inc. J.P. Morgan Securities LLC and Citigroup Global Markets Inc. may release any of the securities subject to these lock-up agreements at any time.

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

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Notice to Prospective Investors in the European Economic Area. In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, no offer of shares may be made to the public in that Relevant Member State other than:

- A. to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the underwriters; or
- C. in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require the Company or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with each of the underwriters and the Company that it is a qualified investor within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive.

In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

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

Notice to Prospective Investors in the United Kingdom. In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are qualified investors (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the Order) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

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

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

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

Electronic Offer, Sale and Distribution of Shares. A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute prospectuses electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations. Other than the prospectus in electronic format, the information on these websites is not part of this prospectus or the registration statement of which this prospectus forms a part, has not been approved or endorsed by us or any underwriter in its capacity as underwriter, and should not be relied upon by investors.

Other Relationships. Certain of the underwriters and their affiliates have provided, and may in the future provide, various investment banking, commercial banking and other financial services for us and our affiliates for which they have received, and may in the future receive, customary fees.

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LEGAL MATTERS

The validity of the shares of common stock being offered by this prospectus will be passed upon for us by Cooley LLP, San Diego, California. The underwriters are being represented by Latham & Watkins LLP, San Diego, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017, as set forth in their report which is incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, 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 <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference the information we file with it, which means that we can disclose important information to you by referring you to those documents. Information incorporated by reference is part of this prospectus supplement and the accompanying prospectus. Later information filed with the SEC will update and supersede this information.

We incorporate by reference the documents listed below and any future filings made with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus supplement until the termination of the offering of the shares covered by this prospectus supplement (other than any information furnished under Item 2.02 or Item 7.01 of any current report on Form 8-K and exhibits filed on such form that are related to such items):

our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 8, 2018;

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the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed) filed with the SEC on April 20, 2018;

our Quarterly Reports on Form 10 Q and Form 10-Q/A filed with the SEC on May 7, 2018, August 1, 2018, August 20, 2018 and November 6, 2018;

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our Current Reports on Form 8 K (other than information furnished rather than filed) filed with the SEC on January 11, 2018, January 24, 2018, April 10, 2018, May 18, 2018, June 7, 2018, August 7, 2018, December 10, 2018, January 7, 2019 and January 16, 2019; and

the description of our common stock which is registered under Section 12 of the Exchange Act, in our registration statement on Form 10-12B/A, filed with the SEC on July 9, 2013, 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 at the following address or telephone number:

Investor Relations

Mirati Therapeutics, Inc.

9393 Towne Centre Drive, Suite 200

San Diego, CA 92121

(858) 332-3410

In accordance with Rule 412 of the Securities Act, any statement contained in a document incorporated by reference herein shall be deemed modified or superseded to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement.

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Prospectus

Common Stock

Preferred Stock

Debt Securities

Warrants

From time to time, we may offer and sell any combination of the securities described in this prospectus, either individually or in combination with other securities. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants.

Each time we sell securities pursuant to this prospectus, we will provide the specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as the documents incorporated by reference, before buying any of the securities being offered.

Our common stock is listed on The Nasdaq Global Select Market under the trading symbol MRTX. On September 5, 2018, the last reported sale price of our common stock was \$56.65 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on The Nasdaq Global Select Market or any other securities exchange of the securities covered by the applicable prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading Risk Factors on page 6 of this prospectus and contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

This prospectus may not be used to consummate a sale of securities unless accompanied by a prospectus supplement.

The securities may be sold directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution in this prospectus. If any agents, underwriters or dealers are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents, underwriters or dealers and any applicable fees, commissions, discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive

from such sale will also be set forth in a prospectus supplement.

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

The date of this prospectus is September 6, 2018.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a shelf registration process. Under this shelf registration process, we may offer and sell shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination with other securities, in one or more offerings. There is no limit on the aggregate amount of the securities that we may offer pursuant to the registration statement of which this prospectus is a part. This prospectus provides you with a general description of the securities we may offer.

Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. We urge you to read carefully this prospectus, any applicable prospectus supplement and any free writing prospectuses we have authorized for use in connection with a specific offering, together with the information incorporated herein by reference as described under the heading **Incorporation of Certain Information by Reference**, before buying any of the securities being offered.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

We have not authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so.

The information appearing in this prospectus, any applicable prospectus supplement and any related free writing prospectus is accurate only as of the date on the front of the document and any information we have 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, the applicable prospectus supplement or any related free writing prospectus, or any sale of a security. Our business, financial condition, results of operations and prospects may have changed since those dates.

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

Unless the context indicates otherwise, as used in this prospectus, the terms **Mirati**, **the Company**, **we**, **us** and **our** to Mirati Therapeutics, Inc., a Delaware corporation, and its subsidiaries on a consolidated basis. Our logos, **Mirati Therapeutics** and **MethylGene**, are unregistered trademarks or service marks of Mirati, and are our property. This prospectus also includes references to trademarks and service marks of other entities, and those trademarks and service marks are the property of their respective owners.

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PROSPECTUS SUMMARY

This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference in this prospectus, and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading Risk Factors contained herein, in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Overview

Company Overview

Mirati Therapeutics, Inc. is a clinical-stage oncology company developing product candidates to address the genetic, epigenetic and immunological promoters of cancer. Our precision oncology clinical programs utilize next-generation genomic testing to identify and select cancer patients who we believe would be most likely to benefit from targeted drug treatment. In immuno-oncology, we are advancing clinical programs where we believe our product candidates have the potential to improve the immune environment of tumor cells and enhance and expand the efficacy of existing cancer immunotherapy medicines when given in combination. Our preclinical programs include potentially first-in-class and best-in-class product candidates specifically designed to address mutations and tumors where few treatment options exist. We approach each of our discovery and development programs with a singular focus: to translate our deep understanding of the molecular drivers of cancer into better therapies and better outcomes for patients.

Our clinical pipeline consists of two clinical-stage product candidates: sitravatinib and mocetinostat. We also have a KRAS inhibitor program in preclinical development.

Sitravatinib in Combination with Immune Checkpoint Inhibitors

Sitravatinib is a spectrum-selective kinase inhibitor that potently inhibits receptor tyrosine kinases, or RTKs, including TAM family receptors (TYRO3, Axl, Mer), split family receptors (VEGFR2, KIT) and RET. As an immuno-oncology agent, sitravatinib is being evaluated in a Phase 2 clinical trial in combination with nivolumab (OPDIVO®), Bristol Myers Squibb's anti-PD-1 checkpoint inhibitor, in patients with non-small cell lung cancer, or NSCLC, who have experienced documented disease progression following prior treatment with a checkpoint inhibitor.

We expect to hold an end of Phase 2 meeting with the U.S. Food and Drug Administration, or FDA, in the third quarter of 2018 with respect to the development of sitravatinib in combination with a checkpoint inhibitor in NSCLC. We plan to present data from this clinical trial at the 2018 European Society of Medical Oncologists Congress, or ESMO, in October 2018, and at the 2018 Society for Immunotherapy of Cancer, or SITC, in November 2018.

We initiated a clinical trial evaluating sitravatinib in combination with nivolumab (OPDIVO®) in patients with head and neck squamous cell cancer in the third quarter of 2018. We also expect to initiate a clinical trial evaluating sitravatinib in combination with nivolumab (OPDIVO®) in patients with bladder cancer in the third quarter of 2018, with additional plans to initiate pre-surgical studies for patients with RCC in the third quarter of 2018.

Sitravatinib as a Single Agent

Sitravatinib is also being evaluated as a single agent in a Phase 1b expansion clinical trial in patients with NSCLC and other tumor types who have specific genetic alterations in CBL, CHR4Q12 and RET. We plan to present data from this clinical trial at ESMO in October 2018.

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Sitravatinib Development in Collaboration with BeiGene, Ltd.

In January 2018, we entered into a Collaboration and License Agreement, or the BeiGene Agreement, with BeiGene, Ltd., or BeiGene, pursuant to which we and BeiGene agreed to collaboratively develop sitravatinib in Asia (excluding Japan and certain other countries), Australia and New Zealand, or the Licensed Territory. Under the BeiGene Agreement, we granted BeiGene an exclusive license to develop, manufacture and commercialize sitravatinib in the Licensed Territory, and we retained exclusive rights for the development, manufacturing and commercialization of sitravatinib outside the Licensed Territory.

We expect that BeiGene will initiate clinical trials evaluating sitravatinib in combination with tislelizumab, BeiGene's clinical-stage PD-1 checkpoint inhibitor, in the fourth quarter of 2018, in patients with NSCLC, RCC, hepatocellular cancer, gastric cancer and ovarian cancer.

Mocetinostat

Mocetinostat is an oral, Class 1 selective histone deacetylase, or HDAC, inhibitor. Mocetinostat is being evaluated in a Phase 2 clinical trial in combination with durvalumab (IMFINZI), MedImmune Limited's anti-PD-L1 checkpoint inhibitor, for the treatment of patients with NSCLC who have experienced disease progression following prior treatment with a checkpoint inhibitor. We expect to report data from this clinical trial later in 2018.

KRAS Inhibitor Program

Our KRAS inhibitor program is focused on the development of compounds that target forms of KRAS which harbor either G12C or G12D mutations. Our lead KRAS G12C compound, MRTX849, is a potent and orally bio-available small molecule and is designed to selectively inhibit G12C mutations. KRAS G12C mutations are present in approximately 14% of NSCLC adenocarcinoma patients and 5% of colorectal cancer, or CRC, patients as well as a small percentage of other tumors (e.g. pancreatic). Tumors characterized by KRAS G12C mutations are commonly associated with poor prognosis and resistance to therapy, and patients with these mutations have few treatment options. Single agent treatment with MRTX849 has shown complete regression of KRAS G12C-positive human tumors implanted in mice. Investigational New Drug application, or IND, enabling pre-clinical studies are underway, and we plan to file an IND in the fourth quarter of 2018. We expect to initiate a Phase 1 clinical trial evaluating MRTX849 in the first quarter of 2019 and to enroll only patients whose tumors carry G12C mutations. Following dose escalation, we expect to expand into cohorts that include patients with NSCLC, CRC and other tumors that carry the G12C mutation. We expect to report early clinical results in 2019.

Corporate Information

We were incorporated in Delaware in April 2013. Our principal executive offices are located at 9393 Towne Centre Drive, Suite 200, San Diego, California 92121, and our telephone number is (858) 332-3410. Our corporate website address is www.mirati.com. We do not incorporate by reference into this prospectus the information on, or accessible through, our website, and you should not consider it as part of this prospectus.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012. We expect to remain an emerging growth company until December 31, 2018.

Description of Securities

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination with other securities, from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of any offering. This

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prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities offering, including, to the extent applicable:

designation or classification;

aggregate principal amount or aggregate offering price;

maturity date, if applicable;

original issue discount, if any;

rates and times of payment of interest or dividends, if any;

redemption, conversion, exercise, exchange or sinking fund terms, if any;

ranking;

restrictive covenants, if any;

voting or other rights, if any;

conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange; and

material or special U.S. federal income tax considerations, if any.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the documents we have incorporated by reference.

We may sell the securities directly to investors or to or through agents, underwriters or dealers. If we do offer securities to or through agents or underwriters, we will include in the applicable prospectus supplement:

the names of those agents or underwriters;

applicable fees, discounts and commissions to be paid to them;

details regarding over-allotment or other options, if any; and

the net proceeds to us, if any.

Common Stock. We may issue shares of our common stock from time to time. The holders of common stock are entitled to one vote per share on all matters to be voted on by the stockholders. Subject to the preferences of any outstanding shares of preferred stock, the holders of common stock are entitled to receive ratably any dividends our board of directors declares out of funds legally available for the payment of dividends. If we are liquidated, dissolved or wound up, the holders of common stock are entitled to share pro rata all assets remaining after payment of liabilities and liquidation preferences of any outstanding shares of preferred stock. Holders of common stock have no preemptive rights or rights to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. In this prospectus, we have summarized certain general features of the common stock under the heading *Description of Capital Stock Common Stock*. We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred Stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our amended and restated certificate of incorporation, our board of directors has the authority to designate up to 10,000,000 shares of preferred stock in one or more series and determine or alter the designation, rights, preferences, privileges and restrictions granted to or imposed upon any series of preferred stock, any or all of

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which may be greater than the rights of the common stock. If we sell any new series of preferred stock under this prospectus and any applicable prospectus supplement, our board of directors will determine the rights, preferences and privileges of the preferred stock being offered, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, voting rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Preferred stock may be convertible into our common stock or other securities of ours, or may be exchangeable for debt securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of the certificate of designation that describes the terms of the series of preferred stock being offered before the issuance of the related series of preferred stock. In this prospectus, we have summarized certain general features of the preferred stock under the heading "Description of Capital Stock - Preferred Stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. Convertible or exchangeable debt securities will be convertible into or exchangeable for our common stock or our other securities. Conversion or exchange may be mandatory or optional (at our option or the holder's option) and would be at prescribed conversion or exchange prices.

The debt securities will be issued under an indenture that we will enter into with a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities under the heading "Description of Debt Securities." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indenture and any supplemental indentures that contain the terms of the debt securities. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or in combination with common stock, preferred stock and/or debt securities offered by any prospectus supplement. In this prospectus, we have summarized certain general features of the warrants under the heading "Description of Warrants." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the warrants. We have filed the forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that we may offer as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Warrants may be issued under a warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if any, in the applicable prospectus supplement relating to a particular series of warrants.

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Use of Proceeds

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we intend to use the net proceeds from the sale of the securities under this prospectus for general corporate purposes, which may include funding research and development, capital expenditures, working capital and general and administrative expenses. See Use of Proceeds on page 7 of this prospectus.

Nasdaq Global Select Market Listing

Our common stock is listed on The Nasdaq Global Select Market under the symbol MRTX.

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RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the heading Risk Factors contained in the applicable prospectus supplement and any related free writing prospectus, and described under the section entitled Risk Factors contained in our most recent annual report on Form 10-K, as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with a specific offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our securities to decline, resulting in a loss of all or part of your investment. Please also carefully read the section below entitled Forward-Looking Statements.

FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act that involve a number of risks and uncertainties. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as believes, expects, hopes, may, will, plan, intends, estimates, could, should, would, continue, seeks, pro forma, or antic words (including their use in the negative), or by discussions of future matters such as the development of new products, technology enhancements, possible collaborations, possible changes in legislation and other statements that are not historical. These statements include but are not limited to statements under the captions Business, Risk Factors and Management's Discussion and Analysis of Financial Condition and Results of Operations and in other sections incorporated by reference from our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as applicable, as well as our other filings with the SEC. You should be aware that the occurrence of any of the events discussed under the heading Risk Factors in any applicable prospectus supplement and any documents incorporated by reference herein or therein could substantially harm our business, operating results and financial condition and that if any of these events occurs, it could adversely affect the value of an investment in our securities.

The cautionary statements made in this prospectus are intended to be applicable to all related forward-looking statements wherever they may appear in this prospectus or in any prospectus supplement or any documents incorporated by reference herein or therein. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

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The following table sets forth our ratio of earnings to fixed charges and the ratio of our combined fixed charges and preference dividends to earnings for each of the periods indicated. The following table is qualified by the more detailed information appearing in the computation table set forth in Exhibit 12.1 to the registration statement of which this prospectus is part and the historical financial statements, including the notes to those financial statements, incorporated by reference in this prospectus. We have paid no dividends on preferred shares during the periods indicated. Therefore, the ratios of earnings to combined fixed charges and preferred dividends are the same as the ratios of earnings to fixed charges.

| | Year Ended December 31, | | | | | Six Months Ended June 30, |
|---|--------------------------------|--------------------|--------------------|--------------------|--------------------|--|
| | 2013 | 2014 | 2015 | 2016 | 2017 | 2018 |
| Ratio of earnings to fixed charges | N/A ⁽¹⁾ | N/A ⁽¹⁾ | N/A ⁽¹⁾ | N/A ⁽¹⁾ | N/A ⁽¹⁾ | N/A ⁽¹⁾ |
| Ratio of earnings to combined fixed charges and preferred stock dividends | N/A ⁽¹⁾ | N/A ⁽¹⁾ | N/A ⁽¹⁾ | N/A ⁽¹⁾ | N/A ⁽¹⁾ | N/A ⁽¹⁾ |

For purposes of computing the ratio of earnings to fixed charges and the ratio of our combined fixed charges and preference dividends to earnings, earnings consist of income (loss) from continuing operations before income taxes plus fixed charges. Fixed charges consist of an estimate of the interest within rental expense.

- (1) We did not generate earnings for the six months ended June 30, 2018 or any of the years ended December 31, 2017, 2016, 2015, 2014 and 2013. Accordingly, our earnings were insufficient to cover fixed charges for such periods and we are unable to disclose a ratio of earnings to fixed charges for such periods. The dollar amount of the deficiency in earnings available for fixed charges for the six months ended June 30, 2018 and the years ended December 31, 2017, 2016, 2015, 2014 and 2013 was approximately \$43 million, \$70 million, \$83 million, \$65 million, \$44 million and \$53 million, respectively.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Unless otherwise indicated in any prospectus supplement, we intend to use the net proceeds from the sale of the securities under this prospectus for general corporate purposes, which may include clinical trial and other research and development expenses, capital expenditures, working capital and general and administrative expenses, and potential acquisitions of or investments in businesses, products and technologies that complement our business, although we have no present commitments or agreements to make any such acquisitions or investments. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus. Pending these uses, we intend to invest the net proceeds in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

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DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our amended and restated certificate of incorporation authorizes us to issue 100,000,000 shares of common stock, par value \$0.001 per share, and 10,000,000 shares of preferred stock, par value \$0.001 per share. As of June 30, 2018, 32,313,440 shares of common stock were outstanding and no shares of preferred stock were outstanding.

The following summary description of our capital stock is based on the provisions of our amended and restated certificate of incorporation, as well as our bylaws and the applicable provisions of the Delaware General Corporation Law. This information is qualified entirely by reference to the applicable provisions of our amended and restated certificate of incorporation, amended and restated bylaws and the Delaware General Corporation Law. For information on how to obtain copies of our amended and restated certificate of incorporation and amended and restated bylaws, which are exhibits to the registration statement of which this prospectus is a part, see [Where You Can Find More Information](#).

Common Stock

Each holder of common stock is entitled to one vote for each share of common stock held on all matters submitted to a vote of the stockholders, including the election of directors. Our amended and restated certificate of incorporation and bylaws do not provide for cumulative voting rights. Other than as described below, holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that are outstanding or that we may designate and issue in the future. All of our outstanding shares of common stock are fully paid and nonassessable.

Preferred Stock

Pursuant to our amended and restated certificate of incorporation our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or stock exchange listing rules), to designate and issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the designations, powers, preferences, privileges and relative participating, optional or special rights and the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, voting rights, terms of redemption and liquidation preferences, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

The preferred shares may have voting or conversion rights that could have the effect of restricting dividends on our shares of common stock, diluting the voting power of our shares of common stock, impairing the rights of our shares of common stock in the event of our dissolution, liquidation or winding-up or otherwise adversely affect the rights of holders of our shares of common stock. The issuance of preferred shares, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change of control and may adversely affect the market price of our shares of common stock and may preclude stockholders from realizing a potential premium over the market value of their shares.

Our board of directors will fix the designations, voting powers, preferences, rights, qualifications, limitations and restrictions of each series of preferred stock that we offer under this prospectus and applicable prospectus supplements in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which

this prospectus is a part, or will incorporate by reference from reports that we file with the

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SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering. This description will include:

the title and stated value;

the number of shares we are offering;

the liquidation preference per share;

the purchase price per share;

the dividend rate per share, dividend period and payment dates and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

our right, if any, to defer payment of dividends and the maximum length of any such deferral period;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock or other securities of ours, including depositary shares and warrants, and, if applicable, the conversion period, the conversion price, or how it will be calculated, and under what circumstances it may be adjusted;

whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange period, the exchange price, or how it will be calculated, and under what circumstances it may be adjusted;

voting rights, if any, of the preferred stock;

preemption rights, if any;

restrictions on transfer, sale or other assignment, if any;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material or special United States federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;

any limitations on issuances of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock being issued as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and

any other specific terms, rights, preferences, privileges, qualifications or restrictions of the preferred stock. The General Corporation Law of the State of Delaware, the state of our incorporation, provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an amendment to our amended and restated certificate of incorporation if the amendment would change the par value or, unless the amended and restated certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

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Board Observer and Nomination Rights

Under the terms of the securities purchase agreement entered into in November 2012, or the 2012 Agreement, entities affiliated with Tavistock Life Sciences, LLC, or Tavistock, may have board observer and nomination rights. As long as Tavistock beneficially owns at least 10% of our issued and outstanding shares of common stock, calculated on a partially diluted basis (assuming only the exercise of any convertible securities or rights to acquire shares of common stock of such stockholders), then Tavistock has the right to appoint an observer to our board of directors. The observer has the right to receive notice of and attend the meetings of our board of directors, and has the right to address our board of directors at any of its meetings, but does not have any right to vote at any meeting of our board of directors. In addition to appointing an observer, as long as Tavistock owns at least 10% of the issued and outstanding shares of common stock, calculated on a partially diluted basis (assuming only the exercise of any convertible securities or rights to acquire shares of common stock of such stockholders), then Tavistock has the right, but not the obligation, to nominate one person to our board of directors. We are required to include Tavistock's director nominee in our proposed slate of directors at each annual or special (if applicable) meeting and recommend that stockholders vote in favor of such nominee.

Under the terms of an agreement entered into in November 2017 that superseded rights under the 2012 Agreement, entities affiliated with Baker Bros. Advisors L.P., or Baker Bros., may have board observer and nomination rights. As long as Baker Bros. beneficially owns at least 3,000,000 shares of our common stock, then Baker Bros. has the right to appoint an observer to our board of directors. The observer has the right to receive notice of and attend the meetings of our board of directors, and has the right to address our board of directors at any of its meetings, but does not have any right to vote at any meeting of our board of directors. In addition to appointing an observer, as long as Baker Bros. owns at least (a) 3,000,000 shares of our common stock and (b) 8% of the issued and outstanding shares of our common stock, calculated on a partially diluted basis (assuming only the exercise of any convertible securities or rights to acquire shares of common stock of such stockholders), then Baker Bros. has the right, but not the obligation, to nominate one person to our board of directors. We are required to include Baker Bros.'s director nominee in our proposed slate of directors at each annual or special (if applicable) meeting and recommend that stockholders vote in favor of such nominee.

Anti-takeover Effects of Provisions of Delaware Law and Charter Documents

Our amended and restated certificate of incorporation and bylaws contain provisions that might have an anti-takeover effect. These provisions, which are summarized below, may have the effect of delaying, deterring or preventing a change in control of our company. They could also impede a transaction in which our stockholders might receive a premium over the then-current market price of our common stock and our stockholders' ability to approve transactions that they consider to be in their best interests.

Our amended and restated certificate of incorporation permits our board of directors to issue preferred stock. We could authorize the issuance of a series of preferred stock which would grant to holders preferred rights to our assets upon liquidation, the right to receive dividend coupons before dividends would be declared to holders of shares of our existing preferred stock and our existing preferred stock and common stock. Our current stockholders have no redemption rights. In addition, as we have a large number of authorized but unissued shares, our board of directors could issue large blocks of voting stock to fend off unwanted tender offers or hostile takeovers without further stockholder approval. We are subject to Section 203 of the Delaware General Corporation Law. In general, Section 203, subject to specific exceptions, prohibits a publicly held Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder, unless:

prior to that date, the board of directors approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85 percent of the voting stock of the corporation

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outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding those shares owned by directors, officers and specific employee stock plans; or

on or after that date, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of the holders of at least $66\frac{2}{3}$ percent of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 defines business combination to include:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, lease, exchange, mortgage, transfer, pledge or other disposition of 10 percent or more of the assets of the corporation involving the interested stockholder;

subject to limited exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;

any transaction involving the corporation that has the effect of increasing the proportionate share of the corporation's stock of any class or series beneficially owned by the interested stockholder; and

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, an interested stockholder is an entity or individual who, together with affiliates and associates, owns, or within three years prior to the determination of the interested stockholder status owned, 15 percent or more of a corporation's outstanding voting stock. The provisions of Section 203 could encourage companies interested in acquiring us to negotiate in advance with our board of directors since the stockholder approval requirement would be avoided if our board of directors approves either the business combination or the transaction that results in the stockholder becoming an interested stockholder. These provisions also could have the effect of preventing changes in our management or could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. The transfer agent and registrar's address is 250 Royall Street, Canton, MA, 02021. The transfer agent for any series of preferred stock that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

Listing on The Nasdaq Global Select Market

Our common stock is listed on The Nasdaq Global Select Market under the symbol MRTX.

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

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We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We have filed the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture does not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as discount securities, which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with original issue discount, or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in the applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

the title of the series of debt securities;

any limit upon the aggregate principal amount that may be issued;

the maturity date or dates;

the form of the debt securities of the series;

the applicability of any guarantees;

whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;

whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price 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 another security or the method by which any such portion shall be determined;

the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;

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our right, if any, to defer payment of interest and the maximum length of any such deferral period;

if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;

the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;

the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;

any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;

whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depositary for such global security or securities;

if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holder's option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;

if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;

additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;

additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;

additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;

additions to or changes in the provisions relating to satisfaction and discharge of the indenture;

additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;

the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;

whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;

the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a United States person for federal tax purposes;

any restrictions on transfer, sale or assignment of the debt securities of the series; and

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any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events of Default under the Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;

if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;

if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and

if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default

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regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

the direction so given by the holder is not in conflict with any law or the applicable indenture; and

subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding. A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

the holder has given written notice to the trustee of a continuing event of default with respect to that series;

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and

the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;

to comply with the provisions described above under the heading Description of Debt Securities Consolidation, Merger or Sale;

to provide for uncertificated debt securities in addition to or in place of certificated debt securities;

to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;

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, as set forth in the indenture;

to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;

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to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under the heading "Description of Debt Securities - General" to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;

to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

extending the fixed maturity of any debt securities of any series;

reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or

reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

provide for payment;

register the transfer or exchange of debt securities of the series;

replace stolen, lost or mutilated debt securities of the series;

pay principal of and premium and interest on any debt securities of the series;

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the trustee;

compensate and indemnify the trustee; and

appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture provides that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depository named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

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At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or

register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we

otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

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All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

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

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplement and free writing prospectus, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be offered independently or in combination with common stock, preferred stock or debt securities offered by any prospectus supplement. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectus, and the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms of the series of warrants being offered, including:

the offering price and aggregate number of warrants offered;

the currency for which the warrants may be purchased;

if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;

in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at, and currency in which, this principal amount of debt securities may be purchased upon such exercise;

in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which these shares may be purchased upon such exercise;

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the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;

the terms of any rights to redeem or call the warrants;

any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

the dates on which the right to exercise the warrants will commence and expire;

the manner in which the warrant agreements and warrants may be modified;

a discussion of material or special U.S. federal income tax considerations, if any, of holding or exercising the warrants;

the terms of the securities issuable upon exercise of the warrants; and

any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or

in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus

supplement, we will, as soon as practicable, issue and deliver the securities purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and any warrant agreements will be governed by and construed in accordance with the internal laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent, if any, will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

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Outstanding Warrants to Purchase Common Stock

As of June 30, 2018, there were warrants to purchase 11,817,912 shares of common stock outstanding. Each of these warrants entitles the holder to purchase one share of common stock at a price of \$0.001 per share of common stock.

LEGAL OWNERSHIP OF SECURITIES

We may issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee, depository or warrant agent maintain for this purpose as the holders of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as indirect holders of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository's book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Securities issued in global form will be registered in the name of the depository or its participants. Consequently, for securities issued in global form, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a book-entry security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository's book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities in non-global form. In these cases, investors may choose to hold their securities in their own names or in street name. Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those

securities.

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Legal Holders

Our obligations, as well as the obligations of any applicable trustee and of any third parties employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depository participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of the indenture or for other purposes. In such an event, we would seek approval only from the holders, and not the indirect holders, of the securities. Whether and how the holders contact the indirect holders is up to the holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form or in street name, you should check with your own institution to find out:

the performance of third-party service providers;

how it handles securities payments and notices;

whether it imposes fees or charges;

how it would handle a request for the holders' consent, if ever required;

whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;

how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and

if the securities are in book-entry form, how the depository's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under the section entitled *Special Situations When a Global Security Will Be Terminated* in this prospectus. As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

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If the prospectus supplement for a particular security indicates that the security will be issued in global form only, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations for Global Securities

The rights of an indirect holder relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only in the form of a global security, an investor should be aware of the following:

an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;

an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;

an investor may not be able to pledge his or her interest in a global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;

the depository's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;

we and any applicable trustee have no responsibility for any aspect of the depository's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depository in any way;

the depository may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and

financial institutions that participate in the depository's book-entry system, and through which an investor holds its interest in a global security, may also have their own policies affecting payments, notices and other

matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When a Global Security Will Be Terminated

In a few special situations described below, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own name, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, the global security will terminate when the following special situations occur:

if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;

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if we notify any applicable trustee that we wish to terminate that global security; or

if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

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PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, at-the-market offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through one or more underwriters or dealers (acting as principal or agent), through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

the name or names of the underwriters, dealers or agents, if any;

the purchase price of the securities or other consideration therefor, and the proceeds, we will receive from the sale;

any over-allotment or other options under which underwriters may purchase additional securities from us;

any agency fees or underwriting discounts and other items constituting agents or underwriters compensation;

any public offering price;

any discounts or concessions allowed or reallocated or paid to dealers; and

any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement will be underwriters of the securities offered by the prospectus supplement. Dealers and agents participating in the distribution of the securities may be deemed to be underwriters, and compensation received by them on resale of the securities may be deemed to be underwriting discounts. If such dealers or agents were deemed to be underwriters, they may be subject to statutory liabilities under the Securities Act.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any over-allotment option. If a dealer is used in the sale of securities, we or an underwriter will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale. To the extent required, we will set forth in the prospectus supplement the name of the dealer and the terms of the transaction. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time.

We may use underwriters, dealers or agents with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, dealer or agent, the nature of any such relationship.

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We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities and we will describe any commissions payable to the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, the agent will act on a best-efforts basis for the period of its appointment.

We may provide agents, underwriters and dealers with indemnification against civil liabilities, including liabilities under the Securities Act, or contribution with respect to payments that the agents, underwriters or dealers may make with respect to these liabilities. Agents, underwriters and dealers, or their affiliates, may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities.

Any underwriter may engage in over-allotment, stabilizing transactions, short-covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum price. Syndicate-covering or other short-covering transactions involve purchases of the securities, either through exercise of the over-allotment option or in the open market after the distribution is completed, to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters that are qualified market makers on The Nasdaq Global Select Market may engage in passive market making transactions in the common stock on The Nasdaq Global Select Market in accordance with Regulation M under the Exchange Act, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and the applicable prospectus supplement.

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LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon by Cooley LLP, San Diego, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our consolidated financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth or incorporated by reference in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference into this prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, 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 <http://www.sec.gov>. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference information from other documents that we file with it, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus. Information in this prospectus supersedes information incorporated by reference that we filed with the SEC prior to the date of this prospectus, while information that we file later with the SEC will automatically update and supersede the information in this prospectus. We incorporate by reference into this prospectus and the registration statement of which this prospectus is a part the information or documents listed below that we have filed with the SEC (Commission File No. 001-35921):

our Annual Report on Form 10-K for the year ended December 31, 2017, which was filed with the SEC on March 8, 2018;

the information specifically incorporated by reference into our Annual Report on Form 10-K for the year ended December 31, 2017 from our definitive proxy statement relating to our 2018 annual meeting of stockholders, which was filed with the SEC on April 20, 2018;

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our Quarterly Reports on Form 10-Q filed with the SEC on May 7, 2018 and August 1, 2018, and our Quarterly Report on Form 10-Q/A filed with the SEC on August 20, 2018;

our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on January 11, 2018, January 24, 2018, April 10, 2018, May 18, 2018, June 7, 2018 and August 7, 2018; and

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the description of our common stock which is registered under Section 12 of the Exchange Act, in our registration statement on Form 10-12B/A, filed with the SEC on July 9, 2013, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will furnish without charge to each person, including any beneficial owner, to whom a prospectus is delivered, upon written or oral request, a copy of any or all of the documents incorporated by reference, including exhibits to these documents. You should direct any requests for documents by writing us at 9393 Towne Centre Drive, Suite 200, San Diego, California 92121 or telephoning us at (858) 332-3410.

**DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR
SECURITIES ACT LIABILITY**

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the registrant pursuant to the foregoing provisions, the registrant has been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable.

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\$75,000,000

COMMON STOCK

PRE-FUNDED WARRANTS TO PURCHASE COMMON STOCK

J.P. Morgan Citigroup Cowen Barclays Credit Suisse