

Mirati Therapeutics, Inc.
Form 424B5
January 28, 2015

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**Filed Pursuant to Rule 424(b)(5)
Registration Statement No. 333-198678**

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has become effective by rule of the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting offers to buy these securities, in any state or other jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JANUARY 28, 2015

PRELIMINARY PROSPECTUS SUPPLEMENT

(To Prospectus dated September 24, 2014)

Shares

Common Stock

We are offering _____ shares of our common stock. Our common stock is listed on The NASDAQ Capital Market under the symbol "MRTX". On January 27, 2015, the last reported sale price for our common stock on The NASDAQ Capital Market was \$20.98 per share.

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

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

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

(1) We have agreed to reimburse the underwriters for certain expenses. See "Underwriting."

The underwriters expect to deliver the shares to purchasers on or about _____, 2015 through the book-entry facilities of The Depository Trust Company.

Joint Book-Running Managers

Citigroup

Jefferies

Leerink Partners

January , 2015

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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 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 24, 2014, 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 biopharmaceutical company focused on developing a pipeline of targeted oncology products. We focus our development programs on drugs intended to treat specific genetically defined subsets of cancer patients with unmet needs. Our pipeline consists of three product candidates: MGCD265, MGCD516 and mocetinostat. MGCD265 and MGCD516 are orally-bioavailable, spectrum-selective kinase inhibitors with distinct target profiles that are in development to treat patients with non-small cell lung cancer, or NSCLC, and other solid tumors including squamous cell carcinoma of the head and neck, or HNSCC. MGCD265 is in Phase 1b clinical development and MGCD516 is in Phase 1 clinical development in the dose escalation phase. Mocetinostat is an orally-bioavailable, spectrum-selective histone deacetylase, or HDAC, inhibitor currently in Phase 2 development. Mocetinostat is being developed for the second line treatment of patients with bladder cancer and non-hodgkins lymphoma, or NHL, specifically focusing on diffuse large B-cell lymphoma, or DLBCL, and follicular lymphoma, or FL. DLBCL and FL tumors have a genetic alteration in one of two genes that have been shown to increase the sensitivity of their tumor cells to mocetinostat in preclinical models.

We believe that an increased understanding of the genomic factors that drive tumor cell growth can lead to the development of cancer drugs that target these genomic factors, resulting in increased efficacy while reducing side effects. We are leveraging this knowledge to develop targeted cancer therapies to address unmet needs in selected cancer patient populations. Our novel kinase inhibitors are intended to target specific mutations that drive the growth of cancer or are implicated in cancer drug resistance or pathogenic processes such as tumor angiogenesis. Our HDAC inhibitor, mocetinostat, acts through important epigenetic mechanisms that are dysregulated in treating certain cancers. We plan to identify additional opportunities by leveraging our deep scientific understanding of molecular drug targets and mechanisms of resistance and potentially in-licensing or internally discovering promising, early-stage novel drug candidates.

Our three clinical stage product candidates are as follows:

MGCD265 is an orally-bioavailable, potent, small molecule kinase inhibitor of MET and Axl receptor tyrosine kinases, or RTKs. MGCD265 is in development for the treatment of solid tumors, with an initial focus on NSCLC but including other solid tumors including gastroesophageal cancers and HNSCC. In 2014 we completed development of a new formulation to improve plasma exposure thereby improving the degree of target inhibition to levels which we believe can be sufficient to demonstrate single agent clinical activity in patients with genetic alterations of MET and Axl. In late 2014 we established the maximum tolerated dose, or MTD, for the new formulation and initiated dose expansion cohorts in patients selected for certain genetic driver mutations that activate the MET and Axl pathways. The patient selection strategy based upon these genetic mutations is designed to result in a high response rate that could enable an accelerated development pathway. We expect to have data regarding clinical proof of

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concept by mid-2015 and, if positive, begin a single-arm registration trial in the second half of 2015.

MGCD516 is an orally-bioavailable, potent, small molecule spectrum-selective kinase inhibitor in development for the treatment of solid tumors with an emphasis on genetic alterations involving the Trk, RET and DDR RTK families. We plan to focus on solid tumors exhibiting genetic alterations or dysregulation of these key drivers of tumor growth, initially in NSCLC. In addition, we plan to evaluate other tumor types where the profile of MGCD516 would suggest clinical benefit. An ongoing Phase 1/1b dose escalation study is designed to identify the optimal biologic dose or MTD and evaluate a cohort of patients selected for key driver mutations in Trk, RET and DDR receptor families. Based upon preclinical and early clinical information, we believe that we will reach a dose that potently inhibits the targeted genetic alterations in the first half of 2015 and initiate dose expansion cohorts in selected patients in mid-2015. We believe that initial data on clinical activity in patients with genetic alterations of Trk, RET or DDR family members could be available in the second half of 2015.

Mocetinostat is an orally-bioavailable, spectrum-selective HDAC inhibitor in Phase 2 clinical trials in patients with bladder cancer, myelodysplastic syndrome, or MDS, and NHL, specifically DLBCL and FL. Patients in the bladder cancer and NHL Phase 2 studies are selected for tumors with genetic alteration in two histone acetyl transferase genes, or HATs, that regulate histone acetylation and that have been shown to increase the sensitivity of tumor cells to mocetinostat in preclinical models. We are also evaluating mocetinostat for the first line treatment of patients with MDS in combination with Vidaza, a hypomethylating agent, or HMA. We believe that this is the first and only ongoing clinical development plan for an HDAC inhibitor in a genetically selected subset of patients. We have completed 13 clinical trials with mocetinostat which enrolled approximately 450 patients with a variety of hematologic malignancies and solid tumors. We expect to see initial proof of concept clinical data in bladder cancer and DLBCL by mid-2015, which, if positive, could enable the initiation of single agent registration trials.

Our Strategy

Our goal is to be a leading developer of targeted cancer therapies for genetically selected patient populations. The key components of our strategy include:

Develop a pipeline of targeted cancer therapies. We believe that an increased understanding of the genomic factors that drive tumor cell growth will lead to the development of cancer drugs with increased efficacy while reducing side effects. We are leveraging the prior successful experience of certain members of our management team in the development and approval of targeted oncology drugs (crizotinib or Xalkori) to develop targeted cancer therapies to address unmet needs in specific cancer populations. Our clinical pipeline is comprised of two novel kinase inhibitors that target specific mutations that drive cancer cell growth and an HDAC inhibitor which is one of the most advanced epigenetic therapies in development. We plan to identify additional targets by leveraging our deep scientific understanding of molecular drug targets and mechanisms of resistance through internal drug discovery activities or potentially in-licensing promising, early-stage novel drug candidates.

Employ efficient and flexible approaches to accelerate clinical development. We will pursue indications and select specific patient populations in which activity of our product candidates can be assessed in small proof of concept, or POC, clinical trials leading to accelerated clinical development. When designing clinical trials, we structure our clinical development approach to test multiple clinical hypotheses in a single trial and design trials with the flexibility to adapt quickly and accelerate once a signal of clinical benefit is observed. We believe our approach may

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increase the likelihood of seeing results early in clinical trials with fewer patients, reducing our clinical development risk and development costs and allowing us to potentially accelerate the development of our product pipeline.

Advance our two lead kinase inhibitors. Kinase inhibitors have significantly improved the care of many cancer patients and represent a commercially successful category of targeted cancer therapies with global sales of over \$29.1 billion in 2011, according to BCC Research. We have two internally discovered novel kinase inhibitors in development: MGCD265 and MGCD516. These product candidates target pathways of high scientific interest, including MET, Axl, Trk, RET, and DDR RTK families and are believed to be drivers of tumor growth and responsible for the development of tumor resistance to several anti-cancer treatments. MGCD265 is in Phase 1b development and MGCD516 is in Phase 1 development in the dose escalation portion of the trial. In the second half of 2015, we expect to initiate a registration trial for MGCD265 following POC and initiate dose expansion cohorts for MGCD516 in selected patients once we achieve a dose at which we are confident our targets are sufficiently inhibited.

Advance mocetinostat, our HDAC inhibitor. HDAC inhibitors have been shown to be effective in treating hematologic malignancies, as evidenced by the approvals of Istodax and Zolinza. We have completed 13 clinical trials with mocetinostat in approximately 450 patients. We are focused on the development of mocetinostat in the treatment of bladder cancer and NHL, specifically DLBCL and FL in patients whose tumors have certain genetic alterations in one of two genes that regulate histone acetylation, CREBBP and EP300. Certain alterations in the CREBBP and EP300 genes have been shown to increase the sensitivity of tumor cells or cancer models to mocetinostat in preclinical studies. We are also evaluating mocetinostat for the first line treatment of patients with MDS in combination with Vidaza, an HMA. Phase 2 trials of single agent mocetinostat in bladder cancer and NHL (DLBCL and FL) are ongoing. We expect initial proof of concept clinical data in bladder cancer patients and DLBCL patients by the mid-2015.

Leverage partnerships to develop our product candidates. We plan to collaborate with third parties and partner certain rights to our product candidates as a means to accelerate their broader clinical development and maximize their therapeutic and market potential. We plan to retain certain key development and commercialization rights in our partnerships. We believe that retaining this strategic flexibility will enable us to maximize shareholder value.

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Product Candidates

The following chart depicts the current state of our oncology development programs:

PRODUCT CANDIDATE	INDICATION	TARGETS	COMMERCIAL RIGHTS	STAGE OF DEVELOPMENT AND ANTICIPATED MILESTONES
MGCD265	Solid Tumors	MET, Axl	Mirati: Global	Initial data from Phase 1b expansion cohorts in selected patients in mid-2015 Initiate Registration Trial in second half of 2015
MGCD516	Solid Tumors	Trk, RET, DDR	Mirati: Global	Phase 1 dose escalation ongoing.
Mocetinostat	Bladder Cancer and NHL (DLBCL and FL)	HDACs 1, 2, 3, 11	Taiho: Certain Asian Territories	Initiate expansion cohorts in second half of 2015. Phase 2 in bladder cancer ongoing. Phase 2 in DLBCL and FL ongoing.
			Mirati: All Other Territories	Initial POC data in bladder in mid-2015. Initial POC data in DLBCL in mid-2015.

Financial Update

While we have not finalized our full financial results for the fiscal year ended December 31, 2014, we expect to report that we had approximately \$29.3 million of cash, cash equivalents and short-term investments as of December 31, 2014. 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, 2014. Additional information and disclosures would be required for a more complete understanding of our financial position and results of operations as of December 31, 2014.

Corporate Information

We were incorporated in Delaware in April 2013. Our principal executive offices are located at 9363 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 will remain an emerging growth company until the earliest of (1) December 31, 2018, (2) the last day of the fiscal year (a) in which we have total annual gross revenue of at least \$1.0 billion, or (b) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700.0 million as of the prior June 30th, and (3) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

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The Offering

Common stock offered by us	shares	
Common stock to be outstanding immediately after this offering	shares	
Option to purchase additional shares		We have granted the underwriters an option to purchase up to additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.
Use of proceeds		We intend to use the net proceeds from this offering for general corporate purposes, which may include clinical trial and other research and development expenses for our ongoing oncology clinical development programs, including acceleration of expenses related to clinical trial activities for the registration of MGCD265, capital expenditures, working capital and general and administrative expenses. See "Use of Proceeds."
Risk factors		Investing in our common stock involves a high degree of risk. See "Risk Factors."
NASDAQ Capital Market listing		Our common stock is listed on The NASDAQ Capital Market under the symbol "MRTX".

The number of shares of our common stock to be outstanding immediately after this offering is based on 13,536,929 shares outstanding as of September 30, 2014, and excludes as of that date:

1,460,017 shares of common stock issuable upon the exercise of outstanding stock options under our equity incentive plans, with a weighted-average exercise price of \$13.93 per share;

460,887 shares of common stock available for future grants under our 2013 equity incentive plan;

300,000 shares of common stock available for issuance under our 2013 employee stock purchase plan; and

2,465,713 shares of common stock issuable upon the exercise of outstanding warrants at a weighted-average exercise price of \$7.22 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.

Certain of our stock options and warrants have exercise prices denominated in Canadian dollars. Unless otherwise indicated, exercise prices for these securities as of specified dates are based upon the exchange rate between the Canadian dollar and the U.S. dollar as of September 30, 2014, and weighted-average exercise prices over specified periods are based upon average daily exchange rates between the Canadian dollar and the U.S. dollar over such periods.

Certain of our existing stockholders have pre-emptive rights to purchase up to their pro rata share of the shares offered in this offering. While we have offered each of these holders the opportunity to purchase shares in this offering and/or received waivers of these pre-emptive rights with respect to this offering, based on the timing of this offering we may not be able to comply with the advance notice requirements of the pre-emptive rights. In this event, we cannot guarantee that the holders of pre-emptive rights that did not waive such rights would not assert that they are entitled to purchase shares outside of this offering or assert other claims based on a breach of the advance notice requirements under the pre-emptive rights provisions. We believe that the pre-emptive rights of stockholders that have not waived such rights would entitle them to purchase no more than an aggregate of approximately 4% of the shares offered in this offering.

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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, 2013, in our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2014, June 30, 2014 and September 30, 2014, in our Current Report on Form 8-K filed with the SEC on January 28, 2015, 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, 2014, 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.

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NOTE REGARDING 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 "anticipates," or other similar 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.

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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USE OF PROCEEDS

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 shares of common stock 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, which may include clinical trial and other research and development expenses for our ongoing oncology clinical development programs, capital expenditures, working capital and general and administrative expenses. In particular, we may accelerate expenditures related to clinical trial activities for the registration of MGCD265.

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.

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Our common stock has been listed on The NASDAQ Capital Market since July 15, 2013 under the symbol "MRTX". Prior to that date, there was no public market for our common stock in the United States as our common stock was listed on the Toronto Stock Exchange.

On January 27, 2015, the closing price for our common stock as reported on The NASDAQ Capital Market was \$20.98 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 Capital Market 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, 2014		
First Quarter	\$ 25.97	\$ 16.50
Second Quarter	\$ 23.75	\$ 15.86
Third Quarter	\$ 21.58	\$ 15.59
Fourth Quarter	\$ 19.90	\$ 13.69
Year Ending December 31, 2015		
First Quarter (through January 27, 2015)	\$ 22.65	\$ 18.26

As of December 31, 2014, 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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DILUTION

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, 2014 was \$35.7 million, or \$2.64 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 (1) the issuance of _____ shares of common stock in this offering and (2) the receipt of the net proceeds from the sale of _____ shares of common stock in this offering at the public offering price of \$ _____ per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of September 30, 2014 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 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, 2014	\$ 2.64
Increase in net tangible book value per share attributable to new investors purchasing shares 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	\$

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.

The above discussion and table are based on 13,536,929 shares of common stock outstanding as of September 30, 2014, which does not include:

1,460,017 shares of common stock issuable upon the exercise of outstanding stock options as of September 30, 2014, at a weighted-average exercise price of \$13.93 per share;

460,887 shares of common stock reserved for future issuance under the 2013 Equity Incentive Plan as of September 30, 2014;

300,000 shares of common stock reserved for future issuance under the 2013 Employee Stock Purchase Plan as of September 30, 2014; and

2,465,713 shares of common stock issuable upon the exercise of outstanding warrants as of September 30, 2014, at a weighted-average exercise price of \$7.22 per share.

To the extent that outstanding exercisable options or warrants are exercised, you may experience further dilution. If all outstanding exercisable options and warrants with exercise prices below \$ _____ per

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share were exercised, our as adjusted net tangible book value as of September 30, 2014 (calculated on the basis of the assumptions set forth above) would have been approximately \$ million, or approximately \$ per share, causing immediate dilution of \$ per share to new investors purchasing shares in this offering.

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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UNDERWRITING

Citigroup Global Markets Inc., Jefferies LLC and Leerink Partners LLC are acting as joint book-running managers of this offering and Citigroup Global Markets Inc. is acting as representative of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus supplement, each underwriter named below has severally agreed to purchase, and we have agreed to sell to that underwriter, the number of shares set forth opposite the underwriter's name in the following table.

Underwriters	Number of Shares
Citigroup Global Markets Inc.	
Jefferies LLC	
Leerink Partners LLC	
Total	

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the option to purchase additional shares described below) if they purchase any of the shares.

Shares sold by the underwriters to the public will initially be offered at the public offering price set forth on the cover of this prospectus supplement. Any shares sold by the underwriters to securities dealers may be sold at a discount from the public offering price not to exceed \$ per share. If all the shares are not sold at the initial offering price, the underwriters may change the offering price and the other selling terms.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus supplement, to purchase up to additional shares at the public offering price less the underwriting discount. Any shares issued or sold under the option will be issued and sold on the same terms and conditions as the other shares that are the subject of this offering.

We and our executive officers and directors have agreed that, subject to specified limited exceptions, for a period of 90 days from the date of this prospectus supplement, we and they will not, without the prior written consent of the Citigroup Global Markets Inc., dispose of or hedge any shares or any securities convertible into or exchangeable for shares of our common stock. Citigroup Global Markets Inc., in its sole discretion, may release any of the securities subject to these lock-up agreements at any time.

Our common stock is listed on The NASDAQ Capital Market under the trading symbol "MRTX".

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Paid by Mirati Therapeutics, Inc.	
	No Exercise	Full Exercise
Per share	\$	\$
Total	\$	\$

We estimate that our portion of the total expenses of this offering will be \$. We have also agreed to reimburse the underwriters for certain FINRA-related and other expenses incurred by them in connection with this offering in an amount up to \$30,000.

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In connection with the offering, the underwriters may purchase and sell shares in the open market. Purchases and sales in the open market may include short sales, purchases to cover short positions, which may include purchases pursuant to the option to purchase additional shares, and stabilizing purchases.

Short sales involve secondary market sales by the underwriters of a greater number of shares than they are required to purchase in the offering.

"Covered" short sales are sales of shares in an amount up to the number of shares represented by the underwriters' option to purchase additional shares.

"Naked" short sales are sales of shares in an amount in excess of the number of shares represented by the underwriters' option to purchase additional shares.

Covering transactions involve purchases of shares either pursuant to the underwriters' option to purchase additional shares or in the open market in order to cover short positions.

To close a naked short position, the underwriters must purchase shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

To close a covered short position, the underwriters must purchase shares in the open market or must exercise the option to purchase additional shares. In determining the source of shares to close the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

Stabilizing transactions involve bids to purchase shares so long as the stabilizing bids do not exceed a specified maximum.

Purchases to cover short positions and stabilizing purchases, as well as other purchases by the underwriters for their own accounts, may have the effect of preventing or retarding a decline in the market price of the shares. They may also cause the price of the shares to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on The NASDAQ Capital Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

Relationships

The underwriters are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business for which they may receive customary fees and reimbursement of expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (which may include bank loans and credit default swaps) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investments and securities activities may involve securities and instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and short positions in such securities and instruments.

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We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

Notice to Prospective Investors in the European Economic Area

In relation to each member state of the European Economic Area that 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 (the relevant implementation date), an offer of shares described in this prospectus supplement may not be made to the public in that relevant member state other than:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

to fewer than 100 or, if the relevant member state has implemented the relevant provision of the 2010 PD Amending Directive, 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the relevant Dealer or Dealers nominated by us for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive.

For purposes of this provision, the expression an "offer of securities to the public" in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the relevant member state) and includes any relevant implementing measure in the relevant member state. The expression 2010 PD Amending Directive means Directive 2010/73/EU.

The sellers of the shares have not authorized and do not authorize the making of any offer of shares through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the shares as contemplated in this prospectus supplement. Accordingly, no purchaser of the shares, other than the underwriters, is authorized to make any further offer of the shares on behalf of the sellers or the underwriters.

Notice to Prospective Investors in the United Kingdom

This prospectus supplement is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (1) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (2) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (each such person being referred to as a "relevant person"). This prospectus supplement and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

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Notice to Prospective Investors in France

Neither this prospectus supplement nor any other offering material relating to the shares described in this prospectus supplement has been submitted to the clearance procedures of the *Autorité des Marchés Financiers* or of the competent authority of another member state of the European Economic Area and notified to the *Autorité des Marchés Financiers*. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus supplement nor any other offering material relating to the shares has been or will be:

released, issued, distributed or caused to be released, issued or distributed to the public in France; or

used in connection with any offer for subscription or sale of the shares to the public in France.

Such offers, sales and distributions will be made in France only:

to qualified investors (*investisseurs qualifiés*) or to a restricted circle of investors (*cercle restreint d'investisseurs*), in each case investing for their own account, all as defined in, and in accordance with articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French *Code monétaire et financier*;

to investment services providers authorized to engage in portfolio management on behalf of third parties; or

in a transaction that, in accordance with article L.411-2-II-1^o-or-2^o-or 3^o of the French *Code monétaire et financier* and article 211-2 of the General Regulations (*Règlement Général*) of the *Autorité des Marchés Financiers*, does not constitute a public offer (*appel public à l'épargne*).

The shares may be resold directly or indirectly, only in compliance with articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French *Code monétaire et financier*.

Notice to Prospective Investors in Hong Kong

The shares may not be offered or sold in Hong Kong by means of any document other than (1) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), (2) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (3) in other circumstances which do not result in the document being a "prospectus" within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong) and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Notice to Prospective Investors in Japan

The shares offered in this prospectus supplement have not been and will not be registered under the Financial Instruments and Exchange Law of Japan. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, in Japan or to or for the account of any resident of Japan (including any corporation or other entity organized under the laws of Japan), except (1) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (2) in compliance with any other applicable requirements of Japanese law.

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Notice to Prospective Investors in Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (1) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (2) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275 of the SFA, or (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA, in each case subject to compliance with conditions set forth in the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

to an institutional investor (for corporations, under Section 274 of the SFA) or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than S\$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions specified in Section 275 of the SFA;

where no consideration is or will be given for the transfer; or

where the transfer is by operation of law.

Notice to Prospective Investors in Australia

No prospectus or other disclosure document (as defined in the Corporations Act 2001 (Cth) of Australia, or the Corporations Act) in relation to the common stock has been or will be lodged with the Australian Securities & Investments Commission, or ASIC. This document has not been lodged with ASIC and is only directed to certain categories of exempt persons. Accordingly, if you receive this document in Australia:

you confirm and warrant that you are either:

a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;

a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to us which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made;

a person associated with the company under section 708(12) of the Corporations Act; or

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a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act, and to the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor, associated person or professional investor under the Corporations Act any offer made to you under this document is void and incapable of acceptance; and

you warrant and agree that you will not offer any of the common stock for resale in Australia within 12 months of that common stock being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

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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, 2013, 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 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):

our Annual Report on Form 10-K for the fiscal year ended December 31, 2013 and filed with the SEC on March 17, 2014;

the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2013 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed) filed with the SEC on April 17, 2014;

our Quarterly Reports on Form 10-Q filed with the SEC on May 15, 2014, August 8, 2014 and November 10, 2014;

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our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on February 5, 2014, March 21, 2014, April 10, 2014, May 15, 2014, May 23, 2014, June 27, 2014, November 6, 2014 and January 28, 2015; 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.
9363 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

\$150,000,000

**Common Stock
Preferred Stock
Warrants**

From time to time, we may offer up to \$150,000,000 of any combination of the securities described in this prospectus in one or more offerings. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable antidilution provisions.

This prospectus provides a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. A 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 any documents incorporated by reference, before you invest in any of the securities being offered.

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

Our common stock is traded on the Nasdaq Global Market under the symbol "MTRX" On September 23, 2014, the last reported sales price of our common stock was \$17.36 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on the Nasdaq Capital Market or any securities market or other exchange of the securities, if any, covered by the prospectus supplement.

We may sell these securities 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 or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts or 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.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained 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.

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 24, 2014.

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ABOUT THIS PROSPECTUS

This prospectus relates to 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 sell any combination of the securities described in this prospectus in one or more offerings up to a total aggregate offering price of \$150,000,000. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain 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 information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading "Incorporation of Certain Information By Reference," before investing in any of the securities offered.

THIS PROSPECTUS MAY NOT BE USED TO CONSUMMATE A SALE OF SECURITIES UNLESS IT IS ACCOMPANIED BY A PROSPECTUS SUPPLEMENT.

Neither we, nor any agent, underwriter or dealer has authorized any person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus prepared by or on behalf of us or to which we have referred you. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor do this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

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 to which this prospectus relates, and you may obtain copies of those documents as described below under the heading "Where You Can Find More Information."

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SUMMARY

This summary highlights selected information from 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 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 to which this prospectus relates.

Unless the context indicates otherwise, as used in this prospectus, the terms "Mirati," "the Company," "we," "us" and "our" refer 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 Therapeutics, Inc., 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.

Company Overview

We are a clinical-stage biopharmaceutical company focused on developing a pipeline of targeted oncology products. We focus our development programs on drugs intended to treat specific subsets of cancer patients with unmet needs. Our pipeline consists of three product candidates: MGCD265, MGCD516 and mocetinostat. MGCD265 and MGCD516 are orally-bioavailable, multi-targeted kinase inhibitors with distinct target profiles that are in development to treat patients with non-small cell lung cancer, or NSCLC, squamous cell carcinoma of the head and neck, or HNSCC, and other solid tumors. MGCD265 is in Phase 1/2 clinical development and MGCD516 is in Phase 1 clinical development. Mocetinostat is an orally-bioavailable, spectrum-selective histone deacetylase, or HDAC, inhibitor currently in Phase 2 clinical development for multiple indications. Based on prior single agent responses in Non Hodgkin's Lymphoma, or NHL, and promising preclinical work we plan to initiate mocetinostat single agent Phase 2 trials in patients with NHL and bladder cancer in the third or fourth quarter of 2014 in patient populations selected based upon a genetic defect in histone acetylation. We are exploring patient selection strategies in an ongoing Phase 2 dose confirmation trial of mocetinostat in combination with Vidaza in myelodysplastic syndromes, or MDS. We are continuing preparations for a Phase 3 trial in MDS in combination with Vidaza. Our decision to move forward with this trial and the timing of doing so are dependent upon the data from three Phase 2 trials and the establishment of a partnership or collaboration for late-stage development or the availability of financing.

Corporate Information

We were incorporated in Delaware in April 2013. Our principal executive offices are located at 9363 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 will remain an emerging growth company until the earlier of (1) December 31, 2018, (2) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.0 billion, or (b) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700.0 million as of the prior June 30th and (3) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior three-year period.

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The Securities We May Offer

We may offer shares of our common stock and preferred stock, and warrants to purchase any of such securities, up to a total aggregate offering price of \$150,000,000 from time to time in one or more offerings under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the relevant offering. This 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, including, to the extent applicable:

designation or classification;

aggregate offering price;

rates and times of payment of dividends, if any;

redemption, conversion, exchange or sinking fund terms, 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;

ranking, if applicable;

restrictive covenants, if any;

voting or other rights, if any; and

important United States federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement to which this prospectus relates.

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

We may sell the securities directly to investors or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

the names of those underwriters or agents;

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

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details regarding over-allotment options, if any; and

the estimated net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders and do not have cumulative voting rights. Subject to preferences that may be applicable to any outstanding shares of preferred stock, the holders of our common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of legally available funds. Upon our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preferences of any then

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outstanding shares of preferred stock. Our common stock does not carry any preemptive rights enabling a holder to subscribe for, or receive shares of, any class of our common stock or any other securities convertible into shares of any class of our common stock, or any redemption rights.

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, without further action by the stockholders (unless such stockholder action is required by applicable law or the rules of any stock exchange or market on which our securities are then traded), to designate up to 10,000,000 shares of preferred stock in one or more series and to determine the designations, voting powers, preferences and rights of each series of the preferred stock, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series, any or all of which may be greater than the rights of the common stock. Any convertible preferred stock we may issue will be convertible into our common stock or our other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in a certificate of designation relating to that series. We will file as an exhibit to the registration statement to which this prospectus relates, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. We urge you to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Warrants. We may issue warrants for the purchase of common stock and/or preferred stock in one or more series. We may issue warrants independently or together with common stock and/or preferred stock and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered have been filed as exhibits to the registration statement to which this prospectus relates, and supplemental warrant agreements and forms of warrant certificates will be filed as exhibits to the registration statement to which this prospectus relates or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

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RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in our Annual Report on Form 10-K for the year ended December 31, 2013, as updated by our annual, quarterly and other reports and documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement to which this prospectus relates. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations.

SPECIAL NOTE REGARDING 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 "anticipates," or other similar 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.

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

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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 September 2, 2014, 13,534,583 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 amended and restated bylaws and the applicable provisions of the Delaware General Corporation Law. This information is qualified entirely by reference to the applicable provisions of our amended and restated certificate of incorporation, amended and restated bylaws and the Delaware General Corporation Law. 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 to which this prospectus relates, 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 and rights of the each series, as well as the qualifications, limitations or restrictions thereof, of the preferred stock of each series 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 to which this

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prospectus relates, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering. 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;

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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

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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.

Pre-Emptive Rights

Under the terms of the securities purchase agreement entered into in November 2012, or the 2012 Securities Purchase Agreement, and the securities purchase agreement entered into in April 2011, or the 2011 Securities Purchase Agreement, certain investors have preemptive rights with respect to any proposed future issuances of our securities. In the event that we propose to issue any class or series of our equity securities, any voting securities, or any securities convertible or exchangeable into, or entitling purchase of, any of the foregoing, we must provide written notice to each investor that purchased, together with such investor's affiliates, at least CND\$4.0 million (or US\$3.8 million, as converted as of June 30, 2014) of the units sold under the 2012 Securities Purchase Agreement or CND\$3.0 million (or US\$2.8 million, as converted as of June 30, 2014) of the units sold under the 2011 Securities Purchase Agreement, specifying the terms and conditions of the proposed issuance. Each such investor has the right, by written notice within four business days from the date of receipt of our notice, in the case of a private placement, or within two business days from the date of the receipt of our notice in the case of a public offering, to subscribe for up to their pro rata share of offered securities, which share is calculated in proportion to the aggregate holding of securities by such investor in relation to the total number of securities issued and outstanding immediately prior to the issuance of offered securities.

The pre-emptive rights described above continue until, in the case of pre-emptive rights arising under the 2012 Securities Purchase Agreement, November 12, 2016 and, in the case of pre-emptive rights arising under the 2011 Securities Purchase Agreement, April 4, 2015. Such rights do not apply, however, to issuances of securities pursuant to:

our Amended and Restated Stock Option Plan, dated as of May 19, 2010, or our Stock Option Plan; our 2013 Equity Incentive Plan, amended on May 21, 2014, or the 2013 Plan; our 2013 Employee Stock Purchase Agreement, or the ESPP;

any collaboration agreements entered into by us;

a public offering of our securities at a price per security at least 100% greater than the respective subscription price, which is CND\$12.44 (or US\$11.65, as converted as of June 30, 2014) in the case of pre-emptive rights arising under the 2011 Securities Purchase Agreement and CND\$14.50 (or US\$13.58, as converted as of June 30, 2014) in connection with which the securities being sold are listed on the New York Stock Exchange or the NASDAQ Stock Market, for total proceeds of at least CND\$50,000,000 (or US\$46,835,000, as converted as of June 30, 2014) and conducted by a recognized, full service investment banking firm;

in the case of pre-emptive rights arising under the 2012 Securities Purchase Agreement, the exercise of the warrants issued under such agreement; or

in the case of pre-emptive rights arising under the 2011 Securities Purchase Agreement, the exercise of warrants issued under such agreement.

Baker Brothers and Tavistock also have a right to acquire any offered securities that are subject to the pre-emptive rights but which are not otherwise purchased by an eligible investor pursuant to such pre-emptive rights. Each of the Baker Brothers and Tavistock may exercise its right to purchase such shares by stating in its notice of exercise of pre-emptive rights that it will acquire up to its pro rata share of such securities. In the event that either Baker Brothers or Tavistock does not exercise its additional rights, the other such stockholder has the right to acquire the remaining offered securities

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that are subject to the pre-emptive rights but that are not otherwise purchased by the other investors. Under the terms of the 2012 Securities Purchase Agreement, for any investor that qualified for pre-emptive rights or additional rights under the 2011 Securities Purchase Agreement that also qualified for such rights under the 2012 Securities Purchase Agreement, the terms of such investor's pre-emptive rights or additional rights as applied to all shares acquired under the 2011 Securities Purchase Agreement and the 2012 Securities Purchase Agreement are governed solely by the terms of the 2012 Securities Purchase Agreement.

Board Observer and Nomination Rights

As long as either Baker Brothers or 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 Baker Brothers and Tavistock, as the case may be, has the right to appoint an observer to the Board of Directors. Each observer has the right to receive notice of and attend the meetings of the Board of Directors, and has the right to address the Board of Directors at any of its meetings, but does not have any right to vote at any meeting of the Board of Directors. In addition to appointing an observer, as long as either Baker Brothers or 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 Baker Brothers and Tavistock, as the case may be, has the right, but not the obligation, to nominate one person to the Board of Directors. We are required to include each of Baker Brothers' and Tavistock's director nominees 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 outstanding at the time the transaction commenced, excluding for purposes of

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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 66²/₃ 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 Capital Market

Our common stock is listed on the Nasdaq Capital Market under the symbol "MRTX."

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DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, 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 or preferred stock and may be issued in one or more series. Warrants may be issued independently or together with common stock or preferred stock offered by any prospectus supplement, and may be attached to or separate from those securities. 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 that we may offer in more detail in the applicable prospectus supplement and any applicable free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We have filed forms of the warrant agreements as exhibits to the registration statement to which this prospectus relates. We will file as exhibits to the registration statement to which this prospectus relates, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, if any, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

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

the title of such securities;

the offering price or prices and aggregate number of warrants offered;

the currency or currencies 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;

if applicable, the date on and after which the warrants and the related securities will be separately transferable;

if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;

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, and the currency in which, these shares may be purchased upon such exercise;

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;

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the terms of any rights to force the exercise of 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 any material or special United States federal income tax consequences 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 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. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent in connection with the exercise of the warrant.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements, and any claim, controversy or dispute arising under or related to the warrants or warrant agreements, will be governed by and construed in accordance with the laws of the State of New York.

Enforceability of Rights by Holders of Warrants

Each warrant agent 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

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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.

Outstanding Warrants to Purchase Common Stock

As of June 30, 2014, there were warrants to purchase 2,469,333 shares of common stock outstanding, which expire between April 2016 and November 2017. Each of these warrants entitles the holder to purchase one share of common stock at prices ranging between CND\$7.46 (or US\$6.99, as converted as of June 30, 2014) and CND\$8.70 (or US\$8.15, as converted as of June 30, 2014), per share of common stock. Each of these warrants has a net exercise provision under which its holder may, in lieu of payment of the exercise price in cash, surrender the warrant and receive a net amount of shares based on the fair market value of our shares of common stock at the time of exercise of the warrant after deduction of the aggregate exercise price. Each of these warrants also contains provisions for the adjustment of the exercise price and the aggregate number of shares issuable upon the exercise of the warrant in the event of dividends, stock splits, reorganizations and reclassifications and consolidations. Certain of these warrants may be subject to an acceleration of their expiration dates if certain conditions are met.

LEGAL OWNERSHIP OF SECURITIES

We can 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 or depository 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. Global securities will be registered in the name of the depository or its participants. Consequently, for global securities, 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 global 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 legal holders, of the securities.

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Street Name Holders

A global security may be terminated in certain situations as described under " Special Situations When A Global Security Will Be Terminated," or issue securities that are not issued in 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 or any applicable trustee or depository 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 or any such trustee or depository 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.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party 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 legal holder, we have no further responsibility for the payment or notice even if that legal holder is required, under agreements with its 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 an indenture, or for other purposes. In such an event, we would seek approval only from the legal holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations for Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

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.

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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 issue to, 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, The Depository Trust Company, New York, New York, known as 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 "Special Situations When A Global Security Will Be Terminated." As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and legal 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 legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, 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

As an indirect holder, an investor's rights 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 as global securities, 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 the 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 the global security;

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

the depositary may, and we understand that DTC will, require that those who purchase and sell interests in the 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 depositary's book-entry system, and through which an investor holds its interest in the 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, a 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 names, so that they will be direct holders. We have described the rights of holders and street name investors above.

A 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;

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 prospectus supplement. When a global security terminates, the depositary, and neither we nor 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, negotiated transactions, block trades or a combination of these methods. We may sell the securities to or through underwriters or dealers, 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.

We may also sell equity securities covered by the registration statement to which this prospectus relates in an "at the market offering" as defined in Rule 415 under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

on or through the facilities of the Nasdaq Capital Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or

to or through a market maker otherwise than on the Nasdaq Capital Market or such other securities exchanges or quotation or trading services.

Such at-the-market offerings, if any, may be conducted by underwriters acting as principal or agent.

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 any underwriters, dealers or agents, if any;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment 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 reallowed or paid to dealers; and

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

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Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

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. Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may change from time to time.

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

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 we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

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

All securities we 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 overallotment, stabilizing transactions, short covering transactions and penalty bids. Overallotment 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. Short covering transactions involve purchases of the securities 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. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any underwriters who are qualified market makers on the Nasdaq Capital Market may engage in passive market making transactions in the securities on the Nasdaq Capital Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. 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.

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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 appearing in our Annual Report on Form 10-K for the year ended December 31, 2013, as set forth in their report which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our 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 relates to a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement, as well as any other document filed by us with the SEC, at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. You can also request copies of these documents by writing to the SEC and paying a fee for the copying cost. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including Iridium. The address of the SEC website is www.sec.gov.

We maintain a website at www.mirati.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

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INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The documents incorporated by reference into this prospectus contain important information that you should read about us.

The following documents are incorporated by reference into this document:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2013 and filed with the SEC on March 17, 2014;

the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2013 from our definitive proxy statement on Schedule 14A (other than information furnished rather than filed) filed with the SEC on April 17, 2014;

our Quarterly Reports on Form 10-Q filed with the SEC on May 15, 2014 and August 8, 2014;

our Current Reports on Form 8-K (other than information furnished rather than filed) filed with the SEC on February 5, 2014, March 21, 2014, April 10, 2014, May 15, 2014, May 23, 2014 and June 27, 2014; 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.

We also incorporate by reference into this prospectus all documents (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) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of this prospectus until the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents by writing us at 9363 Towne Centre Drive, Suite 200, San Diego, California 92121 or telephoning us at (858) 332-3410.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

**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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Shares

Mirati Therapeutics, Inc.

Common Stock

PROSPECTUS SUPPLEMENT

January , 2015

Citigroup

Jefferies

Leerink Partners
