

SECURITIES AND EXCHANGE COMMISSION

FORM 424B5

Prospectus filed pursuant to Rule 424(b)(5)

Filing Date: 2013-01-17
SEC Accession No. 0001193125-13-016048

(HTML Version on secdatabase.com)

FILER

Trius Therapeutics Inc

CIK: **1356857** | IRS No.: **201320630** | State of Incorpor.: **DE** | Fiscal Year End: **1231**
Type: **424B5** | Act: **33** | File No.: **333-183673** | Film No.: **13535089**
SIC: **2834** Pharmaceutical preparations

Mailing Address
6310 NANCY RIDGE DR
SUITE 105
SAN DIEGO CA 92121

Business Address
6310 NANCY RIDGE DR
SUITE 105
SAN DIEGO CA 92121
858-452-0370

[Table of Contents](#)

Filed Pursuant to Rule 424(b)(5)

Registration No. 333-183673

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been declared effective by 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 where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JANUARY 17, 2013

PRELIMINARY PROSPECTUS SUPPLEMENT

(to Prospectus dated September 11, 2012)

Shares



Common Stock

We are selling _____ shares of our common stock. Our common stock is listed on the NASDAQ Global Market under the symbol "TSRX." The last reported sale price of our common stock on the NASDAQ Global Market on January 16, 2013 was \$5.37 per share.

Investing in our common stock involves a high degree of risk. Please read "[Risk Factors](#)" on page S-5 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

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

	Per Share	Total
Public Offering Price	\$	\$
Underwriting Discounts and Commissions	\$	\$
Proceeds to Trius (Before Expenses)	\$	\$

The underwriters expect to deliver the shares of common stock on or about January _____, 2013. As part of this offering, we have granted the underwriters an option for a period of 30 days to purchase up to an additional _____ shares of our common stock. If the

underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$, and the total proceeds to us, before expenses, will be \$ for this offering.

Concurrently with the sale of shares of our common stock under this prospectus supplement, we are selling shares of our common stock under another prospectus supplement, as more fully described herein. The total proceeds to us, before expenses, and the total underwriting discounts and commissions payable by us in connection with this offering and the concurrent offering, in the aggregate, will be \$ and \$, respectively.

Joint Book-Running Managers

Citigroup

Leerink Swann

Co-Lead Manager

Baird

January , 2013

Table of Contents

You should rely only on the information 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 have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. 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 by Reference.”

TABLE OF CONTENTS

	<u>Page</u>
Prospectus Supplement	
ABOUT THIS PROSPECTUS SUPPLEMENT	S-1
SUMMARY	S-2
RISK FACTORS	S-5
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	S-7
USE OF PROCEEDS	S-9
DILUTION	S-10
MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSEQUENCES FOR CERTAIN NON-U.S. HOLDERS	S-11
UNDERWRITING	S-15
LEGAL MATTERS	S-21
EXPERTS	S-21
WHERE YOU CAN FIND MORE INFORMATION	S-21
INCORPORATION BY REFERENCE	S-21
	<u>Page</u>
Prospectus	
ABOUT THIS PROSPECTUS	1
PROSPECTUS SUMMARY	2
RISK FACTORS	5
SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS	5
SELECTED FINANCIAL DATA	6
RATIOS OF EARNINGS TO FIXED CHARGES	6
USE OF PROCEEDS	7
DESCRIPTION OF CAPITAL STOCK	7
DESCRIPTION OF DEBT SECURITIES	13
DESCRIPTION OF WARRANTS	20
LEGAL OWNERSHIP OF SECURITIES	24
PLAN OF DISTRIBUTION	27
LEGAL MATTERS	29
EXPERTS	29

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, 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.

Concurrently with the sale of shares of our common stock under this prospectus supplement, we are selling _____ shares of our common stock under another prospectus supplement, offered pursuant to Registration Statement No. 333-176621, or the 2011 Registration Statement, and the prospectus dated September 15, 2011 included therein, or the 2011 Base Prospectus. As part of the concurrent offering, we granted the underwriters an option for a period of 30 days to purchase up to an additional _____ shares of our common stock.

All references in this prospectus supplement and the accompanying prospectus to “Trius,” the “Company,” “we,” “us,” “our,” or similar references refer to Trius Therapeutics, Inc., except where the context otherwise requires or as otherwise indicated.

This prospectus supplement, the accompanying prospectus, and the information incorporated herein and therein by reference 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.

SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus supplement and in the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information referred to under the heading "Risk Factors" in this prospectus supplement on page S-5.

Our Business and Technologies

We are a biopharmaceutical company focused on the discovery, development and commercialization of innovative antibiotics for serious infections. We are developing tedizolid phosphate, an intravenous, or IV, and oral antibiotic, for the treatment of serious Gram-positive bacterial infections, for acute bacterial skin and skin structure infections, or ABSSSI, and pneumonia, and subsequently for other indications, including bacteremia. ABSSSI is a new classification for complicated skin and skin structure infections. Tedizolid phosphate, our lead product candidate, is a once daily IV and orally administered second generation oxazolidinone being developed for the treatment of serious Gram-positive infections, including those caused by methicillin-resistant staphylococcus aureus (MRSA). In addition, we are discovering antibiotics for infections caused by Gram-negative bacteria using our structure based discovery platform. Our GyrB/ParE dual target program, or Gyrase-B, has been funded since 2008 under a contract with the National Institute of Allergy and Infectious Diseases, or NIAID, a part of the National Institutes of Health. A second preclinical program has been funded under a contract with Lawrence Livermore National Laboratory, a part of the U.S. Department of Energy's National Nuclear Security Administration.

In December 2011, we reported top line data from our first Phase 3 clinical trial, the ESTABLISH-1 (TR-701-112) study, of the oral dosage form of tedizolid phosphate for the treatment of ABSSSI, and in December 2012, we completed enrollment in our second Phase 3 clinical trial, the ESTABLISH-2 (TR-701-113) study, of the IV to oral transition therapy for the treatment of ABSSSI. We expect to report top line data from this second Phase 3 clinical trial in early 2013. We currently expect to submit a New Drug Application to the Food & Drug Administration, or FDA, for tedizolid phosphate for the treatment of ABSSSI during the second half of 2013. We also plan to initiate a Phase 3 program of tedizolid phosphate for the treatment of pneumonia in 2013 using the same 200 mg, once daily dose of tedizolid phosphate that we are currently testing for skin infections. The FDA has designated tedizolid phosphate as a Qualified Infectious Disease Product for the treatment of ABSSSI as well as for the treatment of pneumonia, which designation will enable us to benefit from certain incentives for the development of new antibiotics, including priority review and eligibility for fast-track status.

In July 2011, we signed an exclusive collaboration and license agreement with Bayer Pharma AG to develop and commercialize tedizolid phosphate in China, Japan and substantially all other countries in Asia, Africa, Latin America and the Middle East, excluding North and South Korea. We are evaluating potential strategic alliances for tedizolid phosphate in Europe.

The funds received under our NIAID contract have covered substantially all of the cost of our preclinical efforts on our Gyrase-B program through December 31, 2012. In 2013, while we expect to receive nominal amounts under our NIAID contract to continue to fund our Gyrase-B program, we expect to use a portion of the proceeds from this offering to fund the majority of the program, including the advancement of our Investigational

Table of Contents

New Drug enabling study efforts such that we can present a Phase 1 ready drug candidate to NIAID for review. If approved by NIAID, we would then be entitled to the remaining funds under the contract as we conduct the Phase 1 study. We estimate that these funds would reimburse us for most of the cost of the Phase 1 study. We expect to initiate a Phase 1 clinical trial of Gyrase-B in 2014.

At December 31, 2012, we estimate that we had cash, cash equivalents and investments totaling \$66.0 million. This amount is preliminary, unaudited, subject to change upon completion of our year-end audit, and may differ from what will be reflected in our audited financial statements as of and for the year ended December 31, 2012. Additional information and disclosures would be required for a more complete understanding of our financial position and results of operations as of December 31, 2012.

Company Information

We were originally incorporated in California in June 2004 and reincorporated in Delaware in December 2007. Our principal executive offices are located at 6310 Nancy Ridge Drive, Suite 105, San Diego, California 92121, and our telephone number is (858) 452-0370. Our website address is www.triusrx.com. The information contained in, or that can be accessed through, our website is not part of this prospectus supplement.

Concurrent Offering

Concurrently with the sale of shares of our common stock under this prospectus supplement, we are selling _____ shares of our common stock under another prospectus supplement, offered pursuant to the 2011 Registration Statement and the 2011 Base Prospectus included therein. As part of the concurrent offering, we granted the underwriters an option for a period of 30 days to purchase up to an additional _____ shares of our common stock.

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks described below and discussed under the section captioned "Risk Factors" contained in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2012, which are incorporated by reference in this prospectus supplement and the accompanying prospectus in their entirety, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference, and in any free writing prospectus that we have authorized for use in connection with this offering. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

Risks Related to This Offering

Management will have broad discretion as to the use of the 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 the concurrent 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.

You will experience immediate and substantial dilution in the net tangible book value per share of the common stock you purchase.

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 in the net tangible book value of the common stock you purchase in this offering and in the concurrent offering. Based on the public offering price of \$ per share, if you purchase shares of common stock in this offering or in the concurrent offering, you will suffer immediate and substantial dilution of \$ per share in the net tangible book value of the common stock. See the section entitled "Dilution" below for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering or in the concurrent offering.

You may experience future dilution as a result of future equity offerings and other issuances of our common stock or other securities. In addition, this offering and future equity offerings and other issuances of our common stock or other securities may adversely affect our common stock price.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock, including convertible debt. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering and in the concurrent offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock or securities convertible into common stock in future transactions may be higher or lower than the price per share in this offering and in the concurrent offering. As of September 30, 2012, 3,888,163 shares of common stock were issuable upon the exercise of outstanding stock options; 1,678,884 shares of common stock were issuable upon the exercise of outstanding warrants; and 1,638,439 shares of common stock were reserved for future issuance under our 2010 plan, directors' plan and 2010 purchase plan. You will incur dilution upon exercise of any outstanding stock options, upon exercise of any outstanding warrants or upon the issuance of shares of common stock under our stock incentive plans.

Table of Contents

In addition, the sale of shares in this offering and in the concurrent offering and any future sales of a substantial number of shares of our common stock in the public market, or the perception that such sales may occur, could adversely affect the price of our common stock. We cannot predict the effect, if any, that market sales of those shares of common stock or the availability of those shares of common stock for sale will have on the market price of our common stock.

Risks Related to Ownership of Our Common Stock

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant influence over matters subject to stockholder approval.

As of January 16, 2013, our executive officers, directors, 5% stockholders and their affiliates own approximately 45% of our outstanding voting stock. Upon completion of this offering and the concurrent offering, our executive officers, directors, 5% stockholders and their affiliates will hold approximately _____ of our outstanding voting stock (assuming no exercise of the underwriters' options within this offering or the concurrent offering to purchase additional shares). Therefore, these stockholders may have the ability to influence us through this ownership position. For example, these stockholders may be able to significantly influence elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may feel are in your best interest as one of our stockholders.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering 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. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

Our ability to obtain additional financing;

Our use of the net proceeds from this offering and the concurrent offering;

Our estimates regarding our cash, cash equivalents and investments as of December 31, 2012 and our expenses, future revenues and capital requirements;

The success and timing of our preclinical studies and clinical trials;

Our ability to obtain and maintain regulatory approval of tedizolid phosphate and any other product candidates we may develop, and the labeling under any approval we may obtain;

Regulatory developments in the United States and foreign countries;

The performance of third-party manufacturers;

Our plans to develop and commercialize our product candidates;

Our ability to obtain and maintain intellectual property protection for our product candidates;

The successful development of our sales and marketing capabilities;

The size and growth of the potential markets for our product candidates and our ability to serve those markets;

The rate and degree of market acceptance of any future products;

The success of competing drugs that are or become available; and

Our ability to attract and retain key scientific or management personnel.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expects,” “plans,” “anticipates,” “believes,” “estimates,” “projects,” “predicts,” “potential” and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading “Risk Factors” on page S-5 of this prospectus supplement and in our SEC filings. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement.

You should read this prospectus supplement, the accompanying prospectus, the documents we have filed with the SEC that are incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

You should rely only on the information contained, or incorporated by reference, in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in

S-7

Table of Contents

connection with this offering. We and the underwriters for this offering and the concurrent offering have not authorized anyone to provide you with different information. The common stock offered under this prospectus supplement and the accompanying prospectus is not being offered in any state where the offer is not permitted. You should not assume that the information contained in this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date on the front of this prospectus supplement or the accompanying prospectus, as applicable, or that any information incorporated by reference in this prospectus supplement or the accompanying prospectus is accurate as of any date other than the date of the document so incorporated by reference. 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.

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the _____ shares of common stock that we are offering in this offering and in the concurrent offering will be approximately \$ _____ million, or approximately \$ _____ million if the underwriters exercise in full the options within this offering and the concurrent offering to purchase an aggregate of _____ additional shares of common stock, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering and the concurrent offering for general corporate purposes, including clinical trial, pre-clinical development and other research and development expenses, capital expenditures, working capital and general and administrative expenses, and potential acquisitions of or investments in businesses, products and technologies that complement our business, although we have no present commitments or agreements to make any such acquisitions or investments.

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, technological advances 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 and the concurrent offering. Accordingly, our management will have broad discretion in the application of these proceeds. Pending these uses, we intend to invest the net proceeds primarily in some combination of government agency and/or corporate securities with the balance of the net proceeds held in money market funds in accordance with our investment policy.

Table of Contents

DILUTION

Our net tangible book value as of September 30, 2012, was approximately \$61.3 million, or \$1.58 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2012. Dilution in net tangible book value per share represents the difference between (i) the amount per share paid by purchasers of shares of common stock in this offering and in the concurrent offering and (ii) the net tangible book value per share of our common stock immediately after this offering and the concurrent offering.

After giving effect to the sale on October 10, 2012 to Terrapin Opportunity, L.P., or Terrapin, of 612,133 shares of our common stock for a purchase price of approximately \$5.72 per share and the sale on December 13, 2012 to Terrapin of 1,122,218 shares of our common stock for a purchase price of approximately \$4.46 per share, our pro forma net tangible book value as of September 30, 2012 would have been approximately \$69.8 million, or \$1.72 per share.

After also giving effect to the sale of _____ shares of our common stock in this offering and in the concurrent offering at the public offering price of \$ _____ per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted pro forma net tangible book value as of September 30, 2012, would have been approximately \$ _____ million, or \$ _____ per share. This represents an immediate increase in pro forma net tangible book value of \$ _____ per share to existing stockholders and immediate dilution in pro forma net tangible book value of \$ _____ per share to investors purchasing our common stock in this offering and in the concurrent offering at the public offering price. The following table illustrates this dilution on a per share basis:

Public offering price per share	\$
Pro forma net tangible book value per share of as September 30, 2012	\$1.72
Increase per share attributable to investors purchasing our common stock in this offering and in the concurrent offering	\$
As adjusted pro forma net tangible book value per share after this offering and the concurrent offering	\$
Dilution per share to investors purchasing our common stock in this offering and in the concurrent offering	\$

If the underwriters exercise in full the options within this offering and the concurrent offering to purchase an aggregate of _____ additional shares of common stock at the public offering price of \$ _____ per share, the as adjusted pro forma net tangible book value after this offering and the concurrent offering would be \$ _____ per share, representing an increase in pro forma net tangible book value of \$ _____ per share to existing stockholders and immediate dilution in pro forma net tangible book value of \$ _____ per share to investors purchasing our common stock in this offering and in the concurrent offering at the public offering price.

The above discussion and table are based on 38,791,538 shares outstanding as of September 30, 2012, and exclude as of that date:

3,888,163 shares of common stock reserved for issuance upon the exercise of outstanding stock options, with a weighted average exercise price of \$4.24 per share;

1,678,884 shares of common stock reserved for issuance upon the exercise of outstanding warrants, with a weighted average exercise price of \$8.46 per share; and

1,638,439 shares of common stock reserved for future issuance under our 2010 plan, directors' plan and 2010 purchase plan.

To the extent that outstanding options or warrants are exercised or we issue shares of common stock under our stock incentive plans, investors purchasing our common stock in this offering and in the concurrent offering will 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.

**MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX
CONSEQUENCES FOR CERTAIN NON-U.S. HOLDERS**

The following summary describes the material U.S. federal income and estate tax consequences of the acquisition, ownership and disposition of common stock acquired in this offering by certain Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income and estate taxes and does not deal with state, local and non-U.S. tax consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances, nor does it address U.S. federal tax consequences other than income and estate taxes. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Internal Revenue Code of 1986, as amended, or the Code, such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, persons subject to the alternative minimum tax, regulated investment companies, real estate investment trusts, “controlled foreign corporations,” “passive foreign investment companies,” corporations that accumulate earnings to avoid U.S. federal income tax, persons that hold our common stock as part of a “straddle,” “hedge,” “conversion transaction,” “synthetic security” or integrated investment or other risk reduction strategy, persons deemed to sell our common stock under the constructive sale provisions of the Code, persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation, partnerships and other pass-through entities, investors in such pass-through entities or entities that are treated as “disregarded entities” for U.S. federal income tax purposes (regardless of places of organization or formation). Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income and estate tax consequences different from those discussed below. We have not requested any ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment).

The following discussion is for general information only and is not tax advice. **Persons considering the purchase of common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income and estate tax consequences in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or non-U.S. tax consequences and the possible application of tax treaties that might change the general provisions discussed below.**

For the purposes of this discussion, a “Non-U.S. Holder” is, for U.S. federal income tax purposes, a beneficial owner of common stock that is not a U.S. Holder. A “U.S. Holder” means a beneficial owner of common stock that is for U.S. federal income tax purposes (i) an individual who is a citizen or resident of the United States, (ii) a corporation or other entity treated as a corporation for U.S. federal income tax purposes created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (iii) an estate the income of which is subject to U.S. federal income taxation regardless of its source or (iv) a trust if it (x) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (y) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person. Furthermore, partnerships or other entities that are treated as partnerships for U.S. federal income tax purposes (regardless of their places of organization or formation), entities that are treated as disregarded entities for U.S. federal income tax purposes (regardless of their places of organization or formation), and partners or investors in such entities are not addressed by this discussion and are, therefore, not considered to be Non-U.S. Holders for the purposes of this discussion.

Table of Contents

Distributions

Distributions, if any, of cash or property made on our common stock to a Non-U.S. Holder of our common stock to the extent made out of our current or accumulated earnings and profits (as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. federal income tax purposes. Dividends paid to a Non-U.S. Holder that are not effectively connected with such holder's conduct of a U.S. trade or business generally will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us or our paying agent with a properly-executed IRS Form W-8BEN, or other appropriate form, certifying the Non-U.S. Holder's entitlement to benefits under that treaty. Such certificate must be provided prior to the payment of dividends and must be updated periodically. In the case of a Non-U.S. Holder that is an entity, Treasury regulations and the relevant tax treaty provide rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends will be treated as paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to such agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If you are eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, you should consult your own tax advisor to determine if you are able to obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS. Non-U.S. holders should consult their tax advisors regarding the possible entitlement to benefits under a tax treaty.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that the Non-U.S. Holder maintains in the United States) if a properly-executed IRS Form W-8ECI, or other appropriate form, stating that the dividends are so connected, is furnished to us or our paying agent (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional "branch profits tax," which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder's effectively connected earnings and profits for the taxable year, subject to certain adjustments. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will first reduce your adjusted tax basis in our common stock as a non-taxable return of capital, but not below zero, and then will be treated as gain and taxed in the same manner as capital gain realized from a sale or other disposition of common stock as described in the next section.

Gain on Disposition of Common Stock

A Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (i) the gain is effectively connected with a trade or business of such holder in the United States (and if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (ii) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (iii) we are or have been a "United States real property holding corporation" within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period preceding such disposition or such holder's holding period.

If you are a Non-U.S. Holder described in (i) above, you will be required to pay tax on the net gain derived from the sale at regular U.S. federal income tax rates, unless a specific treaty exemption applies, and corporate Non-U.S. Holders described in (i) above may be subject to the additional branch profits tax at a 30% rate or such

Table of Contents

lower rate as may be specified by an applicable income tax treaty on their effectively connected earnings and profits for the taxable year, as adjusted for certain items. If you are an individual Non-U.S. Holder described in (ii) above, you will be required to pay a flat 30% tax (or such lower rate specified by an applicable income tax treaty) on the gain derived from the sale, which gain may be offset by U.S. source capital losses (even though you are not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses. With respect to (iii) above, in general, we would be a United States real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our assets. We believe that we are not, and do not anticipate becoming, a United States real property holding corporation, but there can be no assurance that we will not become a United States real property holding corporation in the future. Even if we are treated as a United States real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned directly, indirectly and constructively, no more than five percent of our common stock at all times within the shorter of (a) the five year period preceding the disposition or (b) the holder's holding period and (2) our common stock is "regularly traded," as defined by applicable Treasury regulations, on an established securities market. There can be no assurance that our common stock will continue to qualify as regularly traded on an established securities market.

Information Reporting Requirements and Backup Withholding

Generally, we or certain financial middlemen must report information to the IRS with respect to any dividends we pay on our common stock including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient's country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly-executed IRS Form W-8BEN or otherwise establishes an exemption. The current backup withholding rate is 28%.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or non-U.S., except that backup withholding may be avoided if the holder provides a properly-executed IRS Form W-8BEN or otherwise meets documentary evidence requirements for establishing Non-U.S. Holder status or otherwise establishes an exemption. Generally, U.S. backup withholding will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the U.S. through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. If backup withholding applies to you, you should consult with your own tax advisor to determine if you are able to obtain a tax benefit or credit with respect to such backup withholding.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under the Foreign Account Tax Compliance Act, or FATCA, on certain types of payments made to "foreign financial institutions" and certain other non-U.S. entities. Under this legislation, the failure to comply with additional certification, information reporting and other specified requirements could result in withholding tax being imposed on payments of dividends and sales proceeds to certain Non-U.S. Holders. The legislation imposes a 30% withholding tax on dividends on, and gross proceeds

Table of Contents

from the sale or other disposition of, our common stock paid to a “foreign financial institution” or to a “non-financial foreign entity” (each as defined in the Code) unless (i) the foreign financial institution undertakes certain diligence and reporting obligations, (ii) the non-financial foreign entity either certifies it does not have any substantial U.S. owners or furnishes identifying information regarding each substantial U.S. owner, or (iii) the foreign financial institution or non financial foreign entity otherwise qualifies for an exemption from these rules. In addition, if the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (i) above, it generally must enter into an agreement with the U.S. Treasury Department that requires, among other things, that it undertake to identify accounts held by certain U.S. persons or U.S.-owned foreign entities, annually report certain information about such accounts, and withhold 30% on payments to non-compliant foreign financial institutions and certain other account holders.

Although the withholding rules described above currently apply to applicable payments made after December 31, 2012, proposed Treasury regulations and subsequent IRS guidance provide such rules will apply to payments of dividends on our common stock made on or after January 1, 2014, and to payments of gross proceeds on disposition of our common stock on or after January 1, 2017. The guidance described above will not be effective until it is reflected in final Treasury regulations. Holders of our common stock should consult their tax advisors regarding the effect, if any, of these withholding rules on their ownership and disposition of our common stock.

Federal Estate Tax

An individual Non-U.S. Holder who is treated as the owner of, or has made certain lifetime transfers of, an interest in our common stock will be required to include the value thereof in his or her gross estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise, even though such individual was not a citizen or resident of the United States at the time of his or her death.

THE PRECEDING DISCUSSION OF MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW, AS WELL AS THE TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL, NON-U.S., OR U.S. NON-INCOME OR ESTATE TAX LAWS.

Table of Contents

UNDERWRITING

Citigroup Global Markets Inc. and Leerink Swann LLC are acting as joint book-running managers of this offering and the concurrent offering and as representatives 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.

<u>Underwriter</u>	<u>Number of Shares</u>
Citigroup Global Markets Inc.	
Leerink Swann LLC	
Robert W. Baird & Co. Incorporated	
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 underwriters' 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 initial 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 initial 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.

If the underwriters sell more shares than the total number set forth in the table above, 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. We have also granted to the underwriters an option, exercisable on the same terms, to purchase up to additional shares in connection with the concurrent offering. To the extent any such option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment. Any shares issued or sold under any such option will be issued and sold on the same terms and conditions as the other shares that are the subject of this offering and the concurrent offering.

We and our executive officers and directors and entities affiliated with certain of our directors have agreed, that, for a period of 60 days from the date of this prospectus supplement, we and they will not, without the prior written consent of Citigroup and Leerink Swann, directly or indirectly sell, offer, contract or grant any option to sell (including without limitation any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Exchange Act, or otherwise dispose of any shares of our common stock, options or warrants to acquire shares of our common stock, or securities exchangeable or exercisable for or convertible into shares of our common stock currently or hereafter owned either of record or beneficially (as defined in Rule 13d-3 under the Exchange Act) by such person, or publicly announce an intention to do any of the foregoing. Citigroup and Leerink Swann in their sole discretion may release any of the securities subject to these lock-up agreements at any time without notice. The foregoing restrictions on our ability to sell shares of our common stock are subject to specified exceptions. In addition, the foregoing restrictions on the ability of our executive officers and directors and entities affiliated with certain of our directors to sell shares of our common stock do not apply to certain transactions, including:

the transfer of shares of common stock (i) to a family member or trust, (ii) by gift, will or intestacy, or (iii) to partners, members stockholders of the transferor as part of a distribution or to affiliates under the control of the transferor, subject to specified conditions; and

in the case of our executive officers and directors only, the sale of shares of common stock pursuant to written trading plans established pursuant to Rule 10b5-1 of the Exchange Act that are in effect as of the date of the lock-up agreement.

S-15

Table of Contents

Notwithstanding the foregoing, subject to specified exceptions, if (i) during the last 17 days of the 60-day restricted period, we issue an earnings release or material news or a material event relating to our company occurs; or (ii) prior to the expiration of the 60-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 60-day restricted period, the restrictions described above shall continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event, as applicable, unless Citigroup and Leerink Swann waive, in writing, such extension.

The shares are listed on the Nasdaq Global Market under the symbol “TSRX.”

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 the Company	
	No Exercise	Full Exercise
Per share	\$	\$
Total	\$	\$

We estimate that our portion of the total expenses of this offering and the concurrent offering will be \$, which includes \$100,000 that we have agreed to reimburse the underwriters for fees incurred by them in connection with this offering and the concurrent offering.

In connection with this offering and the concurrent 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 underwriters’ options within this offering and the concurrent offering 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’ options within this offering and the concurrent offering 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’ options within this offering and the concurrent offering to purchase additional shares.

Covering transactions involve purchases of shares either pursuant to the underwriters’ options within this offering and the concurrent offering 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 within this offering and/or the concurrent offering 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 underwriters’ options 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.

S-16

Table of Contents

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 Global Market, in the over-the-counter market or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

In addition, in connection with this offering, some of the underwriters (and selling group members) may engage in passive market making transactions in the shares on the Nasdaq Global Market, prior to the pricing and completion of the offering. Passive market making consists of displaying bids on the Nasdaq Global Market no higher than the bid prices of independent market makers and making purchases at prices no higher than those independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are limited to a specified percentage of the passive market maker's average daily trading volume in the shares during a specified period and must be discontinued when that limit is reached. Passive market making may cause the price of the shares to be higher than the price that otherwise would exist in the open market in the absence of those transactions. If the underwriters commence passive market making transactions, they may discontinue them at any time.

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/or 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/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or 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/or short positions in such securities and instruments.

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

Table of Contents

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 and the accompanying prospectus are 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 (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, or the Order, or (ii) 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.

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 the 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:

- (a) you confirm and warrant that you are either:
 - (i) a “sophisticated investor” under section 708(8)(a) or (b) of the Corporations Act;
 - (ii) 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;
 - (iii) a person associated with the company under section 708(12) of the Corporations Act; or
 - (iv) 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
- (b) you warrant and agree that you will not offer any of the common stock for resale in Australia within 12 months of the 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.

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*

S-18

Table of Contents

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*) and/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°-or-2°-or 3° 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 Switzerland

The shares of our common stock may not be publicly offered, distributed or re-distributed on a professional basis in or from Switzerland and neither this document nor any other solicitation for investments in the shares of our common stock may be communicated or distributed in Switzerland in any way that could constitute a public offering within the meaning of Articles 1156/652a of the Swiss Code of Obligations, or CO. This document may not be copied, reproduced, distributed or passed on to others without our prior written consent. This document is not a prospectus within the meaning of Articles 1156/652a CO and the shares of our common stock will not be listed on the SIX Swiss Exchange. Therefore, this document may not comply with the disclosure standards of the CO and/or the listing rules (including any prospectus schemes) of the SIX Swiss Exchange. In addition, it cannot be excluded that we could qualify as a foreign collective investment scheme pursuant to Article 119 para. 2 Swiss Federal Act on Collective Investment Schemes, or CISA. The shares of our common stock will not be licensed for public distribution in and from Switzerland. Therefore, the shares of our common stock may only be offered and sold to so-called "qualified investors" in accordance with the private placement exemptions pursuant to applicable Swiss law (in particular, Article 10 para. 3 CISA and Article 6 of the implementing ordinance to the CISA). We have not been licensed and are not subject to the supervision of the Swiss Financial Market Supervisory Authority, or FINMA. Therefore, investors in the shares of our common stock do not benefit from the specific investor protection provided by CISA and the supervision of the FINMA.

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 (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) 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.

S-19

Table of Contents

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 (i) pursuant to an exemption from the registration requirements of the Financial Instruments and Exchange Law and (ii) in compliance with any other applicable requirements of Japanese law.

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 (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the SFA, (ii) 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 (iii) 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 Chile

The shares are not registered in the Securities Registry (Registro de Valores) or subject to the control of the Chilean Securities and Exchange Commission (Superintendencia de Valores y Seguros de Chile). This prospectus supplement and other offering materials relating to the offer of the shares do not constitute a public offer of, or an invitation to subscribe for or purchase, the shares in the Republic of Chile, other than to individually identified purchasers pursuant to a private offering within the meaning of Article 4 of the Chilean Securities Market Act (Ley de Mercado de Valores) (an offer that is not "addressed to the public at large or to a certain sector or specific group of the public").

[Table of Contents](#)

LEGAL MATTERS

The validity of the common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Cooley LLP, San Diego, California. Latham & Watkins LLP, San Diego, California, is counsel for the underwriters in connection with this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2011, and the effectiveness of our internal control over financial reporting as of December 31, 2011, as set forth in their reports, which are incorporated by reference in this prospectus supplement and the accompanying prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, 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 BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus. Information contained in this prospectus supplement and the accompanying prospectus and information that we file with the SEC in the future and incorporate by reference in this prospectus supplement and the accompanying prospectus will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (other than Current Reports on Form 8-K furnished under Item 2.02 or Item 7.01 and exhibits filed on such form that are related to such items) we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the prospectus supplement and before the sale of all the securities covered by this prospectus supplement:

our Annual Report on Form 10-K for the year ended December 31, 2011, which was filed on March 14, 2012;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2012, June 30, 2012 and September 30, 2012, which were filed on May 9, 2012, August 7, 2012 and November 7, 2012, respectively;

our Current Reports on Form 8-K which were filed on January 3, 2012, January 23, 2012, January 25, 2012, January 26, 2012, April 12, 2012, May 8, 2012 (other than the portions of the report that are furnished but not filed), May 23, 2012, August 31, 2012, October 9, 2012, December 12, 2012 and January 7, 2013;

Table of Contents

our definitive proxy statement relating to our 2012 annual meeting of stockholders, which was filed on April 12, 2012 (other than the portions thereof which are furnished and not filed); and

the description of our common stock on Form 8-A filed on July 23, 2010.

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Trius Therapeutics, Inc.
6310 Nancy Ridge Drive, Suite 105
San Diego, CA 92121
(858) 452-0370
ATTN: Michael Morneau

S-22

\$77,000,000

TRIUS THERAPEUTICS, INC.

**Common Stock
Preferred Stock
Debt Securities
Warrants**

From time to time, we may offer our common stock, preferred stock, debt securities and/or warrants, either individually or in combination, in one or more offerings in amounts, at prices and on terms that we will determine at the time of the offering, with an aggregate initial offering price of up to \$77,000,000. We may also offer common stock or preferred stock upon conversion of debt securities, common stock upon conversion of preferred stock or common stock, preferred stock or debt securities upon the exercise of warrants. We will provide the specific terms of these offerings and securities in one or more supplements to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus that we authorize 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 that we authorize, as well as any documents incorporated by reference, before buying any of the securities being offered.

Our common stock is traded on the NASDAQ Global Market under the symbol "TSRX." On September 10, 2012, the last reported sale price of our common stock on the NASDAQ Global Market was \$5.69. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on the NASDAQ Global Market or any securities market or other exchange of the securities covered by the applicable prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties referenced under the heading "[Risk Factors](#)" on page 5 of this prospectus as well as those contained or referenced 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.

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

The securities may be sold directly to investors, to or through underwriters or dealers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and in the applicable prospectus supplement. If any underwriters are involved in the sale of any securities offered by this prospectus and any prospectus supplement, their names, and any applicable purchase price, fee, commission or discount arrangement between or among them, and any applicable over-allotment options, will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

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

The date of this prospectus is September 11, 2012

Table of Contents

You should rely only on the information contained or incorporated by reference in this prospectus, any applicable prospectus supplement and any related free writing prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. Unless otherwise specified, references to any free writing prospectus refer to a free writing prospectus that we have authorized to be provided to you in connection with an offering. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing prospectus is accurate as of any date other than the date on the front cover of this prospectus, the prospectus supplement or any related free writing prospectus, as applicable, or that the information contained in any document incorporated by reference is accurate as of any date other than the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

TABLE OF CONTENTS

	Page
About this Prospectus	1
Prospectus Summary	2
Risk Factors	5
Special Note Regarding Forward-Looking Statements	5
Selected Financial Data	6
Ratios of Earnings to Fixed Charges	6
Use of Proceeds	7
Description of Capital Stock	7
Description of Debt Securities	13
Description of Warrants	20
Legal Ownership of Securities	24
Plan of Distribution	27
Legal Matters	29
Experts	29
Where you can Find More Information	29
Incorporation by Reference	29

Unless otherwise mentioned or unless the context requires otherwise, all references in this prospectus to “Trius,” “we,” “our”, “us” or similar references mean Trius Therapeutics, Inc., a Delaware corporation.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using 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 dollar amount of \$77,000,000. Each time we offer securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering and the securities offered. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. We may also add, update or change in the prospectus supplement (and in any related free writing prospectus) any of the information contained in this prospectus or in the documents that we have incorporated by reference into this prospectus. To the extent that any statement that we make in a prospectus supplement or any related free writing prospectus is inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in a prospectus supplement or such free writing prospectus. We urge you to carefully read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the headings “Where You Can Find More Information” and “Incorporation by Reference” before buying any of the securities being offered.

PROSPECTUS SUMMARY

About Our Business

We are a biopharmaceutical company focused on the discovery, development and commercialization of innovative antibiotics for life threatening infections. We are developing tedizolid phosphate, an intravenous, or IV, and oral antibiotic, for the treatment of serious Gram-positive bacterial infections, for acute bacterial skin and skin structure infections, or ABSSSI, and pneumonia, and subsequently for other indications, including bacteremia. ABSSSI is a new classification for complicated skin and skin structure infections. Tedizolid phosphate is an IV and orally administered second generation oxazolidinone. In addition, we are discovering antibiotics for broad spectrum infections using our proprietary discovery platform under two government contracts: one funded by the National Institute of Allergy and Infectious Diseases, or NIAID, a part of the National Institutes of Health; and a second contract with Lawrence Livermore National Laboratory, a part of the U.S. Department of Energy's National Nuclear Security Administration.

In December 2011, we completed our first Phase 3 clinical trial of the oral dosage form of tedizolid phosphate for the treatment of ABSSSI, and in September 2011, we initiated our second Phase 3 clinical trial of the IV to oral transition therapy for the treatment of ABSSSI and we expect to report top-line data on this second Phase 3 clinical trial in early 2013. We currently expect to submit a New Drug Application to the Food & Drug Administration for tedizolid phosphate for the treatment of ABSSSI during the second half of 2013. We have also completed a Phase 1 clinical trial which evaluated the ability of tedizolid phosphate to penetrate into the lung, for potential use in treating lung infections. Based on the results of the study, we plan to initiate a Phase 3 program of tedizolid phosphate for the treatment of pneumonia in the first half of 2013 using the same 200 mg, once daily dose of tedizolid phosphate that we are currently testing for skin infections.

In July 2011, we signed an exclusive collaboration and license agreement with Bayer Pharma AG to develop and commercialize tedizolid phosphate in China, Japan and substantially all other countries in Asia, Africa, Latin America and the Middle East, excluding North and South Korea. We are evaluating potential strategic alliances for tedizolid phosphate in Europe.

Preclinical activities for our GyrB/ParE dual target development program, or Gyrase-B, are funded through Phase 1 clinical trials, subject to achievement of program milestones, by our NIAID contract. We are conducting Investigational New Drug enabling studies for Gyrase-B which has potent activity against Gram-negative and Gram-positive bacterial pathogens. We expect to initiate a Phase 1 clinical trial of Gyrase-B in 2013.

We were originally incorporated as RexC Pharmaceuticals, Inc. in California in June 2004 and changed our name to Rx³ Pharmaceuticals, Inc. in September 2004. We subsequently changed our name to Trius Therapeutics, Inc. in February 2007 and reincorporated in Delaware in December 2007. Our principal executive offices are located at 6310 Nancy Ridge Drive, Suite 105, San Diego, California 92121, and our telephone number is (858) 452-0370. Our website address is www.triusrx.com. The information contained in or that can be accessed through our website is not part of this prospectus. Our filings may be read and copied at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. Information on the operation of the Public Reference Room may be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is www.sec.gov. The references to our internet address and the SEC's internet address do not constitute incorporation by reference of the information contained at those sites.

The name TRIUS THERAPEUTICS is our trademark. All other trademarks and tradenames mentioned in this prospectus are the property of their respective owners.

[Table of Contents](#)

The Securities We May Offer

We may offer shares of our common stock and preferred stock, debt securities and/or warrants, either individually or in combination, with a total value of up to \$77,000,000 from time to time under this prospectus, together with any applicable prospectus supplement, at prices and on terms to be determined by market conditions at the time of 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, 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 principal amount or aggregate offering price;
- maturity, if applicable;
- original issue discount, if any;
- rates and times of payment of interest, dividends or other payments, if any;
- redemption, conversion, exercise, exchange, settlement or sinking fund terms, if any;
- conversion, exchange or settlement prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion, exchange or settlement prices or rates and in the securities or other property receivable upon conversion, exchange or settlement;
- ranking;
- restrictive covenants, if any;
- voting or other rights, if any; and
- certain federal income tax considerations.

A prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. However, no prospectus supplement or free writing prospectus shall offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement.

We may sell the securities directly or through underwriters, dealers or agents. We, and our underwriters, dealers 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;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. Holders of our common stock are entitled to one vote per share for the election of directors and on all other matters that require stockholder approval. Subject to any preferential rights of any then outstanding preferred stock, in the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in the assets

Table of Contents

remaining after payment of liabilities and the liquidation preferences of any then outstanding 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 stockholders, to designate up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges, qualifications and restrictions granted to or imposed upon the preferred stock, including dividend rights, conversion rights, voting rights, rights and terms of redemption, liquidation preference and sinking fund terms, any or all of which may be greater than the rights of the common stock.

We will fix the rights, preferences, privileges, qualifications and restrictions of the preferred stock of each series that we sell under this prospectus and applicable prospectus supplements in a certificate of designation relating to that series. We will incorporate by reference into the registration statement of which this prospectus is a part the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. We urge you to read the prospectus supplement (and any related free writing prospectus) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsubordinated debt that we may have and may be secured or unsecured. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all or some portion of our indebtedness. Any convertible debt securities that we issue will be convertible into or exchangeable for our common stock, preferred stock or other securities of ours. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a trustee for the holders of the debt securities. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the prospectus supplement (and any related free writing prospectus) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. Indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series, from time to time. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from those securities.

The warrants will be evidenced by warrant certificates issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the prospectus supplement (and any related free writing prospectus) related to the series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Complete warrant agreements and warrant certificates containing the terms of the warrants being offered will be filed as exhibits to the registration statement of which the prospectus is a part of or will be incorporated by reference from reports we file with the SEC.

RISK FACTORS

An investment in our securities involves a high degree of risk. Prior to making a decision about investing in our securities, you should carefully consider the risks described in the section entitled “Risk Factors” contained in our most recent quarterly report on Form 10-Q, which has been filed with the SEC and is incorporated by reference in this prospectus, as well as any updates thereto contained in subsequent filings with the SEC or any applicable prospectus supplement or free writing prospectus. If any of these risks were to occur, our business, financial condition or results of operations would likely suffer. In that event, the value of our securities could decline, and you could lose all or part of your investment. The risks and uncertainties we describe are not the only ones facing us. Additional risks not presently known to us or that we currently deem immaterial may also impair our business, financial condition or results of operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Any statements in this prospectus or any applicable prospectus supplement, including the documents that we incorporate by reference herein or therein, about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and are forward-looking statements. In some cases, you can identify forward-looking statements by the following words: “may,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “ongoing” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Many important factors affect our ability to achieve our objectives, including:

- our ability to obtain additional financing;
- our use of the net proceeds, if any, from this offering;
- our estimates regarding expenses, future revenues and capital requirements;
- the success and timing of our preclinical studies and clinical trials;
- our ability to obtain and maintain regulatory approval of torezolid phosphate and any other product candidates we may develop, and the labeling under any approval we may obtain;
- regulatory developments in the United States and foreign countries;
- the performance of third-party manufacturers;
- our plans to develop and commercialize our product candidates;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the successful development of our sales and marketing capabilities;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- the rate and degree of market acceptance of any future products;
- the success of competing drugs that are or become available; and
- our ability to attract and retain key scientific or management personnel.

Table of Contents

In addition, you should refer to the “Risk Factors” section of this prospectus for a discussion of other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified timeframe, or at all.

The information contained in or incorporated by reference in this prospectus is accurate only as of the date of this prospectus or the date of the document so incorporated by reference, as applicable, regardless of the time of delivery of this prospectus or any sale of our securities. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

SELECTED FINANCIAL DATA

The following table sets forth our historical selected financial information. Effective January 1, 2012, we adopted the Financial Accounting Standards Board’s Accounting Standards Update, or ASU, No. 2011-05, Comprehensive Income (Topic 220): *Presentation of Comprehensive Income*, as amended by ASU 2011-12, Comprehensive Income (Topic 220): *Deferral of the Effective Date for Amendments to the Presentation of Reclassifications of Items Out of Accumulated Other Comprehensive Income in Accounting Standards Update No. 2011-05*. These updates revise the manner in which entities present comprehensive income in their financial statements. The following selected financial information revises historical information to illustrate the new presentation required by this pronouncement for the periods presented.

Statements of Comprehensive Loss (In thousands)

	Year Ended December 31,		
	2009	2010	2011
Net loss	\$(22,681)	\$(23,863)	\$(18,250)
Unrealized gain (loss) on available-for-sale securities, net	(12)	—	7
Comprehensive loss	<u>\$(22,693)</u>	<u>\$(23,863)</u>	<u>\$(18,243)</u>

RATIOS OF EARNINGS TO FIXED CHARGES

The following table sets forth our ratio of earnings to fixed charges and the ratio of earnings to combined fixed charges and preference dividends for each of the periods presented:

	Year Ended December 31,					Six Months
	2007	2008	2009	2010	2011	Ended June 30, 2012
Ratio of earnings to fixed charges ^(1,2)	—	—	—	—	—	—

- (1) For purposes of computing the ratio of earnings to fixed charges, earnings consist of our net loss before income tax for the period plus fixed charges. We had no capitalized interest during any period. Fixed charges consist of interest expense on debt outstanding, amortization of debt discount and an estimate of the interest portion of rental expense less losses recognized on early extinguishment of debt. The ratio of earnings to fixed charges was less than one-to-one for each of the periods presented. We have not included a ratio of earnings to combined fixed charges and preferred stock dividends because we do not have any preferred stock outstanding as of the date of this prospectus.

[Table of Contents](#)

- (2) Earnings were insufficient to cover fixed charges by \$8.7 million in 2007, \$20.8 million in 2008, \$22.7 million in 2009, \$23.9 million in 2010, \$18.3 million in 2011, and \$22.0 million in the first six months of 2012.

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 and pre-clinical trial and other research and development expenses, capital expenditures, working capital and general and administrative expenses, and potential acquisitions of or investments in businesses, products and technologies that complement our business, although we have no present commitments or agreements to make any such acquisitions or investments. Pending these uses, we intend to invest the net proceeds primarily in some combination of government agency and/or corporate securities with the balance of the net proceeds held in money market funds in accordance with our investment policy.

DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 200,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share.

The following is a summary of the rights of our common stock and preferred stock. This summary is not complete. For more detailed information, please see our amended and restated certificate of incorporation and amended and restated bylaws, which were filed as exhibits to our Registration Statement on Form S-1 (No. 333- 162945).

Common Stock

Outstanding Shares. On September 10, 2012, there were 38,791,043 shares of common stock outstanding, held of record by approximately 95 stockholders.

As of September 10, 2012, there were 723,787 shares of common stock subject to outstanding options under our 2006 Equity Incentive Plan, 2,937,871 shares of common stock subject to outstanding options under our 2010 Equity Incentive Plan, 227,000 shares of common stock subject to outstanding options under our 2010 Non-Employee Directors' Plan, and up to 1,678,884 shares of common stock subject to outstanding warrants.

Voting Rights. Each holder of common stock is entitled to one vote for each share of common stock on all matters submitted to a vote of the stockholders, including the election of directors. Our amended and restated certificate of incorporation and amended and restated bylaws do not provide for cumulative voting rights. Because of this, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election.

Dividends. Subject to preferences that may be applicable to any then outstanding preferred stock, the holders of common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation. In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities, subject to the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Table of Contents

Rights and Preferences. Holders of common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to our 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 preferred stock that we may designate and issue in the future.

Fully Paid and Nonassessable. All of our outstanding shares of common stock are duly authorized, validly issued, fully paid and nonassessable.

Preferred Stock

Our board of directors is authorized, subject to any limitations prescribed by law, without stockholder approval, to issue from time to time up to an aggregate of 10,000,000 shares of preferred stock, in one or more series. We currently have no shares of preferred stock outstanding. Prior to the issuance of shares of each class or series, our board of directors is required by the Delaware General Corporation Law and our amended and restated certificate of incorporation to adopt resolutions and file a certificate of designation with the Delaware Secretary of State. The certificate of designation fixes for each class or series the designations, powers, preferences, rights, qualifications, limitations and restrictions of that class or series, including the following:

- the number of shares constituting each class or series;
- voting rights;
- rights and terms of redemption, including sinking fund provisions;
- dividend rights and rates;
- terms concerning the distribution of assets;
- conversion or exchange terms;
- redemption prices; and
- liquidation preferences.

All shares of preferred stock offered by this prospectus, when issued and paid for, will be validly issued, fully paid and nonassessable and will not have any preemptive or subscription rights.

We will describe in a prospectus supplement relating to the class or series of any preferred stock being offered the following terms:

- the title and stated value of the preferred stock;
- the number of shares of the preferred stock offered, the liquidation preference per share and the offering price of the preferred stock;
- the dividend rate(s), period(s) or payment date(s) or method(s) of calculation applicable to the preferred stock;
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends on the preferred stock will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for auction and remarketing, if any, for the preferred stock;
- the provisions for a sinking fund, if any, for the preferred stock;
- the provision for redemption, if applicable, of the preferred stock;
- any listing of the preferred stock on any securities exchange;

Table of Contents

the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price or manner of calculation and conversion period;

voting rights, if any, of the preferred stock;

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 upon the liquidation, dissolution or winding up of our affairs;

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs; and

any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

Warrants

As of September 10, 2012, a warrant exercisable for an aggregate of 16,384 shares of our common stock was outstanding and will be exercisable for a period of five years from August 2, 2010. In addition, warrants to purchase 1,662,500 shares of common stock were issued in a private placement transaction that closed on May 31, 2011. Such warrants are exercisable for a period of five years commencing on November 27, 2011. Each of the warrants contains a customary net issuance feature, which allows the warrant holder to pay the exercise price of the warrant by forfeiting a portion of the exercised warrant shares with a value equal to the aggregate exercise price.

Registration Rights

Amended and Restated Investor Rights Agreement

Under our amended and restated investor rights agreement, the holders of 8,478,377 shares of common stock, or their transferees, have the right to require us to register their shares with the SEC so that those shares may be publicly resold, or to include their shares in any registration statement we file. In addition, Forsythe Biotechnology Group, Inc. or its transferee has “piggyback” registration rights as described below with respect to an aggregate of 16,384 shares of common stock issuable upon exercise of warrants held by such entity.

Demand Registration Rights. At any time, the holders of at least 20% of the shares (or the holders of less than 20% so long as the aggregate number of securities requested to be sold under such registration statement is at least \$5,000,000) having demand registration rights have the right to make up to two demands that we file a registration statement, subject to specified exceptions, conditions and limitations, including the right of the underwriters to limit the number of shares included in any such registration under certain circumstances.

Form S-3 Registration Rights. If we are eligible to file a registration statement on Form S-3, one or more holders of registration rights have the right to demand that we file a registration statement on Form S-3 so long as the aggregate amount of securities to be sold under the registration statement on Form S-3 is at least \$1,000,000, subject to specified exceptions, conditions and limitations.

“Piggyback” Registration Rights. If we register any securities for public sale, holders of registration rights will have the right to include their shares in the registration statement. The underwriters of any underwritten offering will have the right to limit the number of shares having registration rights to be included in the registration statement, but not below 20% of the total number of shares included in the registration statement.

Expenses of Registration. Generally, we are required to bear all registration and selling expenses incurred in connection with the demand, piggyback and Form S-3 registrations described above, other than underwriting discounts and commissions.

Table of Contents

Expiration of Registration Rights. The demand, piggyback and Form S-3 registration rights discussed above will terminate five years following the closing of our initial public offering or, as to a given holder of registrable securities, when such holder is able to sell all of their registrable securities in a single 90-day period under Rule 144 of the Securities Act.

Registration Rights with Respect to May 2011 Private Placement

In connection with a private placement of units consisting of common stock and warrants that closed on May 31, 2011, we entered into a registration rights agreement, or the Registration Rights Agreement, with the investors in the private placement. The Registration Rights Agreement required that we file a “resale” registration statement covering all of the shares of common stock and the common stock underlying the warrants issued in the private placement, up to the maximum number of shares able to be registered pursuant to applicable SEC regulations, within 30 days of the closing of the private placement. We filed a “resale” registration statement on Form S-1 with the SEC on June 21, 2011, which was declared effective by the SEC on July 6, 2011 and a post effective amendment thereto onto Form S-3 with the SEC on September 1, 2011, which was declared effective by the SEC on September 15, 2011. Under the terms of the Registration Rights Agreement, we are obligated to maintain the effectiveness of the “resale” registration statement until all securities therein are sold or otherwise can be sold pursuant to Rule 144, without any restrictions. The Registration Rights Agreement contains customary terms and conditions for a transaction of this type, including certain customary cash penalties on us for our failure to satisfy specified filing and effectiveness time periods.

Delaware Anti-Takeover Law and Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and our amended and restated bylaws contain certain provisions that could have the effect of delaying, deterring or preventing another party from acquiring control of us. These provisions and certain provisions of the Delaware General Corporation Law which are summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed, in part, to encourage persons seeking to acquire control of us to negotiate first with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate more favorable terms with an unfriendly or unsolicited acquirer outweigh the disadvantages of potentially discouraging a proposal to acquire us.

Delaware Anti-Takeover Law. We are subject to Section 203 of the Delaware General Corporation Law. Section 203 generally prohibits a public Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a period of three years after the date of the transaction in which the person became an interested stockholder, unless:

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

the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the number of shares outstanding (a) shares owned by persons who are directors and also officers and (b) shares owned by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

on or subsequent to the date of the transaction, the business combination is approved by the board and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock which is not owned by the interested stockholder.

Table of Contents

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; 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, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Amended and Restated Certificate of Incorporation and Bylaws. Among other things, our amended and restated certificate of incorporation and bylaws:

- permit our board of directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (including the right to approve an acquisition or other change in control);
- provide that the authorized number of directors may be changed only by resolution of the board of directors;
- provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by the affirmative vote of a majority of directors then in office, even if less than a quorum;
- divide our board of directors into three classes;
- require that any action to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and not be taken by written consent;
- provide that stockholders seeking to present proposals before a meeting of stockholders or to nominate candidates for election as directors at a meeting of stockholders must provide notice in writing in a timely manner, and also specify requirements as to the form and content of a stockholder's notice;
- do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose); and
- provide that special meetings of our stockholders may be called only by the chairman of the board, our chief executive officer or by the board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors.

The amendment of any of these provisions would require approval by the holders of at least 66 2/3% of our then outstanding common stock.

The provisions of the Delaware General Corporation Law and the provisions of our amended and restated certificate of incorporation and amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they might also inhibit temporary fluctuations in the market price of our securities that often result from actual or rumored hostile takeover attempts. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that security holders might otherwise deem to be in their best interests.

[Table of Contents](#)

Listing on The NASDAQ Global Market

Our shares of common stock are listed on The NASDAQ Global Market under the symbol “TSRX.”

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare. The transfer agent and registrar’s address is 480 Washington Boulevard, Jersey City, New Jersey, 07310.

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements or free writing prospectus, summarizes the material terms and provisions of the debt securities that we may offer under this prospectus. While the terms we have summarized below will generally apply to any future debt securities we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement or free writing prospectus. The terms of any debt securities we offer under a prospectus supplement or free writing prospectus may differ from the terms we describe below.

We will issue any senior notes under a senior indenture which we will enter into with the trustee named in the senior indenture. We will issue any subordinated notes under a subordinated indenture which we will enter into with the trustee named in the subordinated indenture. We have filed forms of these documents as exhibits to the registration statement of which this prospectus is a part. We use the term “indentures” to refer to both the senior indenture and the subordinated indenture.

The indentures will be qualified under the Trust Indenture Act of 1939, as amended. We use the term “debenture trustee” to refer to either the senior trustee or the subordinated trustee, as applicable.

The following summaries of material provisions of the senior notes, the subordinated notes and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplement or free writing prospectus that is related to the debt securities that we sell under this prospectus, as well as the complete indentures that contain the terms of the debt securities. Except as we may otherwise indicate, the terms of the senior indenture and the subordinated indenture are identical.

General

We will describe in the applicable prospectus supplement or free writing prospectus the terms relating to a series of debt securities, including:

the title;

the principal amount being offered, and, if a series, the total amount authorized and the total amount outstanding;

any limit on the amount that may be issued;

whether or not we will issue the series of debt securities in global form and, if so, the terms and who the depository will be;

the maturity date;

the principal amount due at maturity, and whether the debt securities will be issued with any original issue discount;

whether and under what circumstances, if any, we will pay additional amounts on any debt securities held by a person who is not a United States person for tax purposes, and whether we can redeem the debt securities if we have to pay such additional amounts;

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

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

the terms of the subordination of any series of subordinated debt;

Table of Contents

the place where payments will be payable;

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

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

the date, if any, after which, the conditions upon which, and the price at which we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions, and any other applicable terms of those redemption provisions;

provisions for a sinking fund, purchase or other analogous fund, if any;

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

whether the indenture will restrict our ability or the ability of our subsidiaries to:

- incur additional indebtedness;

- issue additional securities;

- create liens;

- pay dividends or make distributions in respect of our capital stock or the capital stock of our subsidiaries;

- redeem capital stock;

- place restrictions on our subsidiaries' ability to pay dividends, make distributions or transfer assets;

- make investments or other restricted payments;

- sell or otherwise dispose of assets;

- enter into sale-leaseback transactions;

- engage in transactions with stockholders or affiliates;

- issue or sell stock of our subsidiaries; or

- effect a consolidation or merger;

whether the indenture will require us to maintain any interest coverage, fixed charge, cash flow-based, asset-based or other financial ratios;

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

information describing any book-entry features;

the procedures for any auction or remarketing, if any;

whether the debt securities are to be offered at a price such that they will be deemed to be offered at an "original issue discount" as defined in paragraph (a) of Section 1273 of the Internal Revenue Code of 1986, as amended;

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

if other than dollars, the currency in which the series of debt securities will be denominated; and

any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, including any events of default that are in addition to those described in this prospectus or any covenants provided with respect to the debt securities that are in addition to those described above, and any terms which may be required by us or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

Table of Contents

Conversion or Exchange Rights

We will set forth in the applicable prospectus supplement or free writing prospectus the terms on which a series of debt securities may be convertible into or exchangeable for common stock, preferred stock or other securities of ours or a third party, including the conversion or exchange rate, as applicable, or how it will be calculated, and the applicable conversion or exchange period. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of our securities or the securities of a third party that the holders of the series of debt securities receive upon conversion or exchange would, under the circumstances described in those provisions, be subject to adjustment, or pursuant to which those holders would, under those circumstances, receive other property upon conversion or exchange, for example in the event of our merger or consolidation with another entity.

Consolidation, Merger or Sale

The indentures in the forms initially filed as exhibits to the registration statement of which this prospectus is a part do not contain any covenant which restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor of ours or acquiror of such assets would have to assume all of our obligations under the indentures and the debt securities, as appropriate.

If the debt securities are convertible for our other securities or securities of other entities, the person with whom we consolidate or merge or to whom we sell all of our property would have to make provisions for the conversion of the debt securities into securities which the holders of the debt securities would have received if they had converted the debt securities before the consolidation, merger or sale.

Events of Default Under the Indenture

The following are events of default under the indentures with respect to any series of debt securities that we may issue:

- if we fail to pay interest when due and payable and our failure continues for 90 days and the time for payment has not been extended or deferred;
- if we fail to pay the principal, premium or sinking fund payment, if any, when due and payable and the time for payment has not been extended or delayed;
- if we fail to observe or perform any other covenant contained in the debt securities or the indentures, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive notice from the debenture trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

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

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Table of Contents

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

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

subject to its duties under the Trust Indenture Act of 1939, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will only have the right to institute a proceeding under the indentures or to appoint a receiver or trustee, or to seek other remedies if:

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

the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and

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

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

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

Modification of Indenture; Waiver

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

to fix any ambiguity, defect or inconsistency in the indenture;

to comply with the provisions described above under “Consolidation, Merger or Sale”;

to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act of 1939, as amended;

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

to evidence and provide for the acceptance of appointment by a successor trustee;

to provide for uncertificated debt securities and to make all appropriate changes for such purpose;

to add to, delete from, or revise the conditions, limitations and restrictions on the authorized amount, terms or purposes of issuance, authorization and delivery of debt securities of any series;

Table of Contents

to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default, or to surrender any of our rights or powers under the indenture; or

to change anything that does not materially adversely affect the interests of any holder of debt securities of any series.

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

extending the fixed maturity of the series of debt securities;

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

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

Discharge

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

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

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

maintain paying agencies;

hold monies for payment in trust;

recover excess money held by the debenture trustee;

compensate and indemnify the debenture trustee; and

appoint any successor trustee.

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

Form, Exchange and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement or free writing prospectus, in denominations of \$1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, New York, New York, known as DTC, or another depository named by us and identified in a prospectus supplement or free writing prospectus with respect to that series. See “Legal Ownership of Securities” for a further description of the terms relating to any book-entry securities.

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

Table of Contents

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

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

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

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

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

Information Concerning the Debenture Trustee

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

Payment and Paying Agents

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

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that, unless we otherwise indicate in the applicable prospectus supplement or free writing prospectus, we may make interest payments by check which we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in a prospectus supplement or free writing prospectus, we will designate an office or agency of the debenture trustee in the City of New York as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement or free writing prospectus any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

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

Table of Contents

Governing Law

The indentures and the debt securities will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

Subordination of Subordinated Debt Securities

The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement or free writing prospectus. The indentures in the forms initially filed as exhibits to the registration statement of which this prospectus is a part do not limit the amount of indebtedness which we may incur, including senior indebtedness or subordinated indebtedness, and do not limit us from issuing any other debt, including secured debt or unsecured debt.

DESCRIPTION OF WARRANTS

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

We may issue the warrants under a warrant agreement which we may enter into with a warrant agent to be selected by us. We use the term “warrant agreement” to refer to any of these warrant agreements. We use the term “warrant agent” to refer to the warrant agent under any of these warrant agreements. The warrant agent will act solely as an agent of ours in connection with the warrants and will not act as an agent for the holders or beneficial owners of the warrants.

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 applicable to a particular series of warrants. We urge you to read the applicable prospectus supplement or free writing prospectus related to the warrants that we sell under this prospectus, as well as the complete warrant agreements that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement or free writing prospectus the terms relating to a series of warrants. If warrants for the purchase of debt securities are offered, the prospectus supplement or a free writing prospectus will describe the following terms, to the extent applicable:

- the offering price and the aggregate number of warrants offered;
- the currencies in which the warrants are being offered;
- the designation, aggregate principal amount, currencies, denominations and terms of the series of debt securities that can be purchased if a holder exercises a warrant;
- the designation and terms of any series of debt securities with which the warrants are being offered and the number of warrants offered with each such debt security;
- the principal amount of the series of debt securities that can be purchased if a holder exercises a warrant and the price at which and currencies in which such principal amount may be purchased upon exercise;
- the terms of any rights to redeem or call the warrants;
- the date on which the right to exercise the warrants begins and the date on which such right expires;
- federal income tax consequences of holding or exercising the warrants; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the warrants.

Warrants for the purchase of debt securities will be in registered form only.

If warrants for the purchase of common stock or preferred stock are offered, the prospectus supplement or a free writing prospectus will describe the following terms, to the extent applicable:

- the offering price and the aggregate number of warrants offered;

Table of Contents

the total number of shares that can be purchased if a holder of the warrants exercises them and, in the case of warrants for preferred stock, the designation, total number and terms of the series of preferred stock that can be purchased upon exercise;

the designation and terms of any series of preferred stock with which the warrants are being offered and the number of warrants being offered with each share of common stock or preferred stock;

the number of shares of common stock or preferred stock that can be purchased if a holder exercises the warrant and the price at which such common stock or preferred stock may be purchased upon exercise, including, if applicable, any provisions for changes to or adjustments in the exercise price and in the securities or other property receivable upon exercise;

the terms of any rights to redeem or call, or accelerate the expiration of, the warrants;

the date on which the right to exercise the warrants begins and the date on which that right expires;

federal income tax consequences of holding or exercising the warrants; and

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

Warrants for the purchase of common stock or preferred stock will be in registered form only.

If the warrants are offered attached to common stock, preferred stock or debt securities, the prospectus supplement or a free writing prospectus will also describe the date on and after which the holder of the warrants can transfer them separately from the related common stock, series of preferred stock or debt securities.

A holder of warrant certificates may exchange them for new certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement or free writing prospectus. Until any warrants to purchase debt securities are exercised, the holder of the warrants will not have any of the rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or to exercise any voting rights, except to the extent set forth under “–Warrant Adjustments” below.

Exercise of Warrants

Each holder of a warrant is entitled to purchase the principal amount of debt securities or number of shares of common stock or preferred stock, as the case may be, at the exercise price described in the applicable prospectus supplement or free writing prospectus. After the close of business on the day when the right to exercise terminates (or a later date if we extend the time for exercise), unexercised warrants will become void.

A holder of warrants may exercise them by following the general procedure outlined below:

- delivering to the warrant agent the payment required by the applicable prospectus supplement or free writing prospectus to purchase the underlying security;
- properly completing and signing the reverse side of the warrant certificate representing the warrants; and
- delivering the warrant certificate representing the warrants to the warrant agent within five business days of the warrant agent receiving payment of the exercise price.

If you comply with the procedures described above, your warrants will be considered to have been exercised when the warrant agent receives payment of the exercise price, subject to the transfer books for the securities issuable upon exercise of the warrant not being closed on such date. After you have completed those procedures

Table of Contents

and subject to the foregoing, we will, as soon as practicable, issue and deliver to you the debt securities, common stock or preferred stock that you purchased upon exercise. If you exercise fewer than all of the warrants represented by a warrant certificate, a new warrant certificate will be issued to you for the unexercised amount of warrants. Holders of warrants will be required to pay any tax or governmental charge that may be imposed in connection with transferring the underlying securities in connection with the exercise of the warrants.

Amendments and Supplements to the Warrant Agreements

We may amend or supplement a warrant agreement without the consent of the holders of the applicable warrants to cure ambiguities in the warrant agreement, to cure or correct a defective provision in the warrant agreement, or to provide for other matters under the warrant agreement that we and the warrant agent deem necessary or desirable, so long as, in each case, such amendments or supplements do not materially and adversely affect the interests of the holders of the warrants.

Warrant Adjustments

Unless the applicable prospectus supplement or free writing prospectus states otherwise, the exercise price of, and the number of securities covered by, a common stock warrant or preferred stock warrant will be adjusted proportionately if we subdivide or combine our common stock or preferred stock, as applicable. In addition, unless the prospectus supplement or a free writing prospectus states otherwise, if we, without receiving payment for:

- issue capital stock or other securities convertible into or exchangeable for common stock or preferred stock, or any rights to subscribe for, purchase or otherwise acquire any of the foregoing, as a dividend or distribution to holders of our common stock or preferred stock;

- pay any cash to holders of our common stock or preferred stock other than a cash dividend paid out of our current or retained earnings or other than in accordance with the terms of the preferred stock;

- issue any evidence of our indebtedness or rights to subscribe for or purchase our indebtedness to holders of our common stock or preferred stock; or

- issue common stock or preferred stock or additional stock or other securities or property to holders of our common stock or preferred stock by way of spinoff, split-up, reclassification, combination of shares or similar corporate rearrangement,

then the holders of common stock warrants and preferred stock warrants, as applicable, will be entitled to receive upon exercise of the warrants, in addition to the securities otherwise receivable upon exercise of the warrants and without paying any additional consideration, the amount of stock and other securities and property such holders would have been entitled to receive had they held the common stock or preferred stock, as applicable, issuable under the warrants on the dates on which holders of those securities received or became entitled to receive such additional stock and other securities and property.

Except as stated above or as otherwise set forth in the applicable prospectus supplement or free writing prospectus, the exercise price and number of securities covered by a common stock warrant and preferred stock warrant, and the amounts of other securities or property to be received, if any, upon exercise of those warrants, will not be adjusted or provided for if we issue those securities or any securities convertible into or exchangeable for those securities, or securities carrying the right to purchase those securities or securities convertible into or exchangeable for those securities.

Holders of common stock warrants and preferred stock warrants may have additional rights under the following circumstances:

- certain reclassifications, capital reorganizations or changes of the common stock or preferred stock, as applicable;

Table of Contents

certain share exchanges, mergers, or similar transactions involving us and which result in changes of the common stock or preferred stock, as applicable; or

certain sales or dispositions to another entity of all or substantially all of our property and assets.

If one of the above transactions occurs and holders of our common stock or preferred stock are entitled to receive stock, securities or other property with respect to or in exchange for their securities, the holders of the common stock warrants and preferred stock warrants then outstanding, as applicable, will be entitled to receive upon exercise of their warrants the kind and amount of shares of stock and other securities or property that they would have received upon the applicable transaction if they had exercised their warrants immediately before the transaction.

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 depositary or warrant agent maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement or free writing prospectus. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depositary on behalf of other financial institutions that participate in the depositary’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 depositary or its participants. Consequently, for global securities, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary 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 depositary 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 depositary’s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not holders, of the securities.

Street Name Holders

We may terminate a global security or issue securities 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 depositary 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 depositary 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.

Table of Contents

For example, once we make a payment or give a notice to the holder, we have no further responsibility for the payment or notice even if that holder is required, under agreements with depository participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of 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 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 global securities, how the depository's rules and procedures will affect these matters.

Global Securities

A global security is a security which 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 or a free writing prospectus, DTC will be the depository for all global securities issued under this prospectus.

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 holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement or a free writing prospectus 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.

Table of Contents

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 legal holder of securities and instead deal only with the depository that holds the global security.

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

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

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

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

An investor may not be able to pledge his or her interest in 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. We and any applicable trustee have no responsibility for any aspect of the depository's actions or for its records of ownership interests in the global security. We and the trustee also do not supervise the depository in any way;

The depository 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 depository'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 name, 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 depository notifies us that it is unwilling, unable or no longer qualified to continue as depository for that global security and we do not appoint another institution to act as depository 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 prospectus supplement or a free writing prospectus 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 or a free writing prospectus. When a global security terminates, the depository, and not we or any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus in any of three ways (or in any combination):

- to or through underwriters or dealers;
- directly to a limited number of purchasers or to a single purchaser; or
- through agents.

The prospectus supplement or a free writing prospectus will set forth the terms of the offering of the securities covered by this prospectus, including:

- the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any underwriting discounts or commissions or agency fees and other items constituting underwriters' or agents' compensation;
- the initial public offering price of the securities and the proceeds to us and any discounts, commissions or concessions allowed or reallocated or paid to dealers; and
- any securities exchanges or markets on which the securities may be listed.

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

Underwriters may offer and sell the offered securities from time to time in one or more transactions, including negotiated 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. If underwriters are used in the sale of any securities, the securities will be acquired by the underwriters for their own account and may be resold from time to time in one or more transactions described above. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters. Generally, the underwriters' obligations to purchase the securities will be subject to certain conditions precedent. The underwriters will be obligated to purchase all of the securities if they purchase any of the securities. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement or a free writing prospectus, naming the underwriter, the nature of any such relationship.

We may sell the securities directly or through agents from time to time. The prospectus supplement or a free writing prospectus will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the securities from us at the public offering price set forth in the prospectus supplement or a free writing prospectus pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The contracts will be subject only to those conditions set forth in the prospectus supplement or a free writing prospectus, and the prospectus supplement or a free writing prospectus will set forth any commissions we pay for solicitation of these contracts.

Agents and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the agents or underwriters may be required to make in respect thereof. Agents and underwriters may be customers of, engage in transactions with, or perform services for us in the ordinary course of business.

Table of Contents

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 over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. 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 covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters who are qualified market makers on the NASDAQ Global Market may engage in passive market making transactions in our common stock, preferred stock, warrants and debt securities, as applicable, on the NASDAQ Global 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.

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

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon for us by Cooley LLP, San Diego, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2011, and the effectiveness of our internal control over financial reporting as of December 31, 2011, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act of 1933, as amended, covering the securities described in this prospectus. This prospectus, which constitutes a part of the registration statement, does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the common stock offered by this prospectus, you should refer to the registration statement and the exhibits filed as part of that document. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

We are subject to the informational requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at <http://www.sec.gov>. You may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC 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 facilities.

INCORPORATION BY REFERENCE

We are incorporating by reference some information about us that we file with the SEC. We are disclosing important information to you by referencing those filed documents. Any information that we reference this way is considered part of this prospectus. The information in this prospectus supersedes information incorporated by reference that we have filed with the SEC prior to the date of this prospectus, while information that we file with the SEC after the date of this prospectus that is incorporated by reference will automatically update and supersede the information in this prospectus.

We incorporate by reference the following documents we have filed, or may file, with the SEC (other than portions of current reports furnished under Item 2.02 or Item 7.01 of Form 8-K or other portions of documents filed with the SEC which are furnished, but not filed, pursuant to applicable rules promulgated by the SEC):

our Annual Report on Form 10-K for the fiscal year ended December 31, 2011 (other than information furnished rather than filed), which was filed on March 14, 2012;

our Quarterly Reports on Form 10-Q for the quarter ended March 31, 2012 and June 30, 2012, which were filed on May 9, 2012 and August 7, 2012, respectively;

Table of Contents

our Current Reports on Form 8-K filed on January 3, 2012, January 23, 2012, January 25, 2012, January 26, 2012, April 12, 2012, May 8, 2012, May 23, 2012 and August 31, 2012;

the description of our common stock contained in the Registration Statement on Form 8-A filed on July 23, 2010; and

all documents filed by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, (i) after the date of the initial filing of the registration statement of which this prospectus is a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus and prior to the termination of the offering.

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

Trius Therapeutics, Inc.
6310 Nancy Ridge Drive, Suite 105
San Diego, California 92121
Tel: (858) 452-0370

Shares



Common Stock

PRELIMINARY PROSPECTUS SUPPLEMENT

January , 2013

Joint Book-Running Managers

Citigroup

Leerink Swann

Co-Lead Manager

Baird
