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The information in this prospectus supplement is not complete and may be changed. This prospectus supplement and the accompanying prospectus are not offers to sell these securities, and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED NOVEMBER 12, 2013

FILED PURSUANT TO RULE 424(B)(5)
REGISTRATION NO. 333-187242

PROSPECTUS SUPPLEMENT
(to Prospectus dated May 1, 2013)

Shares



Common Stock

We are offering _____ shares of our common stock. Our common stock is listed on The NASDAQ Global Market under the symbol "SNTA." The last reported sale price of our common stock on November 11, 2013 was \$4.05 per share.

Investing in our common stock involves a high degree of risk. Please read "Risk Factors" beginning on page S-8 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 passed on the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	<u>Per share</u>	<u>Total</u>
Public Offering Price	\$	\$
Underwriting Discounts and Commissions ⁽¹⁾	\$	\$
Proceeds to Synta, before expenses	\$	\$

(1) The underwriters will be reimbursed for certain expenses incurred in this offering. See "Underwriting" for details.

Delivery of the shares of common stock is expected to be made on or about November _____, 2013. 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 \$ _____.

Sole Book-Running Manager

Jefferies

Prospectus Supplement dated November _____, 2013

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You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering. Neither we nor the underwriters have authorized anyone to provide you with information different from that contained in this prospectus supplement, the accompanying prospectus or any accompanying free writing prospectus. We are offering to sell, and seeking offers to buy, common stock only in jurisdictions where offers and sales are permitted. If anyone provides you with different or inconsistent information, you should not rely on it. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. The information contained in this prospectus supplement, the accompanying prospectus and any accompanying free writing prospectus is accurate only as of the date of this prospectus supplement, the accompanying prospectus and any such accompanying free writing prospectus, regardless of the time of delivery of this prospectus supplement, the accompanying prospectus, any such accompanying free writing prospectus or of any sale of our common stock. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you in the sections of this prospectus supplement entitled "Where You Can Find More Information" and "Incorporation of Documents by Reference."

No action is being taken in any jurisdiction outside the United States to permit a public offering of the common stock or possession or distribution of this prospectus supplement, the accompanying prospectus or any free writing prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement, the accompanying prospectus or any free writing prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement, the accompanying prospectus and any accompanying free writing prospectus applicable to that jurisdiction.

ABOUT THIS PROSPECTUS SUPPLEMENT

On March 14, 2013, we filed with the Securities and Exchange Commission, or SEC, a registration statement on Form S-3 (File No. 333-187242) utilizing a shelf registration process relating to the securities described in this prospectus supplement, which registration statement became effective on May 1, 2013. Under this shelf registration process, we may, from time to time, sell common stock and other securities, of which this offering is a part.

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into the prospectus and this prospectus supplement. The second part, the accompanying prospectus, gives more general information, some of which does not apply to this offering. Generally, when we refer to this prospectus, we are referring to both parts of this document combined.

If the description of the offering varies between this prospectus supplement and the accompanying prospectus, you should rely on the information contained in this prospectus supplement. However, 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.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in

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some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Unless we have indicated otherwise, or the context otherwise requires, references in this prospectus supplement and the accompanying prospectus to "Synta," "the Company," "we," "us" and "our" or similar terms are to Synta Pharmaceuticals Corp. and its subsidiaries.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read this entire prospectus supplement and the accompanying prospectus carefully, including the "Risk Factors" section contained in this prospectus supplement, our consolidated financial statements and the related notes thereto and the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

Overview

Synta Pharmaceuticals Corp. is a biopharmaceutical company focused on discovering, developing, and commercializing small molecule drugs to extend and enhance the lives of patients with severe medical conditions, including cancer and chronic inflammatory diseases. We have two drug candidates in clinical trials for treating multiple types of cancer and several drug candidates in the preclinical stage of development. All of our drug candidates have been discovered and developed internally using our proprietary, unique chemical compound library and integrated discovery engine. We retain full ownership of all of our proprietary rights in our drug candidates.

Oncology Programs

We have two clinical-stage programs and two preclinical-stage programs in oncology:

Ganetespi (Hsp90 Inhibitor)

Ganetespi is a novel, small molecule inhibitor of Hsp90, a molecular chaperone which is required for the proper folding and activation of many cancer-promoting proteins. In preclinical cancer models, inhibition of Hsp90 by ganetespi leads to the simultaneous degradation of many of these proteins and the subsequent death or cell cycle arrest of cancer cells dependent on these proteins for growth. A number of Hsp90 client proteins are also involved in the resistance of cancer cells to other anti-cancer treatments, such as chemotherapy. The ability to reduce cancer-cell drug resistance suggests potential for combining ganetespi with chemotherapies or other anti-cancer agents. In preclinical studies, ganetespi has shown anti-cancer activity against a broad range of solid and hematologic cancers, both as a monotherapy and in combination with certain widely used anti-cancer agents.

Ganetespi has been studied or is currently being evaluated in over 25 clinical trials including our GALAXY-1 and GALAXY-2 trials evaluating ganetespi in combination with docetaxel chemotherapy for patients with second-line, advanced, non-small cell lung cancer (NSCLC) as well as our ENCHANT-1 clinical trial evaluating single-agent ganetespi in patients with locally advanced or metastatic breast cancer. Over 800 patients have been treated with ganetespi to date across ongoing or completed clinical trials. In these trials, ganetespi has shown activity both administered as monotherapy and in combination with chemotherapy.

GALAXY-1 Phase 2b/3 Clinical Trial

In 2011 we initiated the GALAXY-1 trial in patients with advanced NSCLC who received one prior treatment for advanced disease, i.e., a second-line treatment setting. GALAXY-1 compares treatment with docetaxel alone, which is approved for second-line treatment, vs. treatment with ganetespi plus docetaxel. The aims of this study were to:

- evaluate clinical benefit and establish the safety profile of ganetespi in combination with docetaxel relative to docetaxel alone;
- identify the patient populations, by biomarker or other disease characteristics, which may be most responsive to combination treatment; and

- build the clinical and operational experience needed to optimize the design and execution of the pivotal GALAXY-2 Phase 3 trial.

At the World Conference on Lung Cancer in October 2013 we reported results from the interim analysis specified for one year from the date of last patient enrolled, conducted in October, 2013. Highlights from this analysis include:

- 65% of overall survival (OS) events in the primary adenocarcinoma population had occurred. At least 70% of OS events are expected at the time of final analysis, expected by early 2014.
- Consistent with previously reported results, encouraging OS improvements were observed in the prespecified chemosensitive patient population (diagnosis of advanced disease greater than 6 months; N=178), together with a lack of activity in the refractory population. These results continue to support the selection of the chemosensitive patient population for the GALAXY-2 Phase 3 trial.
- OS Hazard Ratio in the chemosensitive population was 0.75 (90% CI 0.56, 1.03; 1-sided p=0.065) and 0.72 (90% C.I. 0.52, 0.98; 1-sided p=0.040) in the Cox proportional hazards univariate (unadjusted) and multivariate (adjusted) models, respectively. Median OS improved from 7.4 months to 10.7 months in the docetaxel (D) vs. ganetespib in combination with docetaxel (G+D) arms, respectively.
- Results for progression-free survival (PFS) were consistent with the improvements observed for OS. PFS Hazard Ratio in the chemosensitive population was 0.73 (90% CI 0.55, 0.96; 1-sided p=0.031) and 0.72 (90% C.I. 0.53, 0.96; 1-sided p=0.03) in the Cox proportional hazards univariate (unadjusted) and multivariate (adjusted) models. Median PFS improved from 3.4 months to 5.3 months, in the D vs. G+D arms, respectively.
- In the refractory population (N=75), which progressed rapidly on or shortly after first-line chemotherapy, no benefit was observed. The OS Hazard ratios were 1.32 (90% CI 0.82, 2.11) and 1.18 (90% CI 0.71, 1.94) in the Cox proportional hazards univariate (unadjusted) and multivariate (adjusted) models, respectively.

The safety profile of adenocarcinoma patients treated with the combination of ganetespib and docetaxel was generally similar to that of docetaxel alone, consistent with previously reported results. A high incidence of visual impairment has been reported following treatment with certain other Hsp90 inhibitors. Consistent with prior findings with ganetespib, reports of visual impairment in this study were infrequent: 2 (2%) in the G+D arm and 0 (0%) in the D arm. Both cases of visual impairment in the G+D arm were transient and were Grade 1.

GALAXY-2 Phase 3 Clinical Trial

In October 2012, we participated in an End-of-Phase 2 (EOP2) meeting with the U. S. Food and Drug Administration (FDA) to review plans for the global, randomized GALAXY-2 Phase 3 clinical trial. We have incorporated comments from this meeting into the protocol.

GALAXY-2 is designed to enroll approximately 500 patients with Stage IIB/IV non-small cell lung adenocarcinoma who received one prior chemotherapy-based regimen for metastatic disease and who were diagnosed with advanced disease at least six months prior to study entry. Enrollment will be stratified to ensure the balance of key prognostic factors including ECOG performance status (0 versus 1), baseline level of lactate dehydrogenase (LDH) (greater versus less than upper limit of normal), and geographic region (North America and Western Europe versus Rest of World).

The GALAXY-2 trial design mirrors the GALAXY-1 trial. Patients will be randomized 1:1 to receive ganetespib plus docetaxel, or docetaxel alone. Docetaxel will be administered at 75 mg/m² on day 1 of a 21-day treatment cycle in both arms until disease progression or treatment intolerance. Patients in the combination arm will also receive ganetespib 150 mg/m² on days 1 and 15 of the 21-day treatment cycle.

In the combination arm, following the completion of docetaxel therapy, treatment with ganetespib alone may be continued until disease progression or treatment intolerance.

The primary endpoint of the GALAXY-2 trial is OS. Two event-driven interim analyses are planned, which will be reviewed by an independent data monitoring committee. Key secondary endpoints include PFS and overall response rate, as well as OS in certain biomarker-defined subpopulations.

The GALAXY-2 protocol specifies that trial size and statistical assumptions may be updated based on final results from GALAXY-1. We are currently reviewing the latest GALAXY-1 results and are considering whether to increase GALAXY-2 trial size from 500 patients to as many as 700 patients. This change is intended to decrease the risk from imbalances or statistical fluctuations.

Enrollment of GALAXY-2 began in April 2013. Assuming a trial size increase to 700 patients, we expect interim analyses to be conducted in the second half of 2014, and the final analysis to be conducted in the first half of 2015.

ENCHANT-1 Phase 2 Clinical Trial

In 2012, we initiated the ENCHANT-1 trial designed to evaluate ganetespib monotherapy as first-line treatment for locally advanced or metastatic HER2+ breast cancer and triple-negative breast cancer (TNBC). The primary endpoint of this study is overall response rate within three treatment cycles (12 weeks).

The ENCHANT-1 trial specified that transition from the first stage (15 evaluable patients per cohort) to the second stage of the trial (up to an additional 18 evaluable patients per cohort) would occur for each cohort if there were at least one objective tumor response in that cohort. In July 2013, we announced that of the initial five HER2+ patients enrolled in the study, two achieved objective tumor response and two achieved stable disease (SD). Of the initial ten TNBC patients enrolled and evaluable for response, two achieved objective tumor response and three achieved SD following treatment with ganetespib monotherapy. One of the responding TNBC patients, who was diagnosed with inoperable TNBC, achieved a complete clinical response following treatment with ganetespib. Her disease was restaged from inoperable to operable and she successfully completed surgery with curative intent. The criteria to advance to the second stage of the ENCHANT-1 trial were achieved in this interim analysis, and enrollment will continue up to a total of 33 evaluable patients per cohort.

Because of the widespread use of taxanes in breast cancer, and results from the GALAXY-1 trial evaluating ganetespib in combination with docetaxel, exploring the combination of taxanes with ganetespib in breast cancer is of high interest. As a result, we have amended the ENCHANT-1 protocol to allow for combination treatment with paclitaxel and ganetespib following 12-weeks of treatment with ganetespib monotherapy.

HER2+ and TNBC represent two major subtypes of breast cancer, each accounting for approximately 15 to 20% of new breast cancer cases. The majority of breast cancers are hormone receptor positive (ER/PR+). The clinical activity observed with ganetespib in HER2+ and TNBC patients supports further evaluation in this remaining major subtype of breast cancer. We have added an additional cohort to the ENCHANT-1 protocol to evaluate ganetespib activity in patients with ER/PR+ breast cancer. The design of this cohort is similar to the design of the other two cohorts.

We expect to present initial results from the ENCHANT-1 trial in December 2013.

Additional Ganetespib Clinical Trials

In addition to the clinical trials we plan to initiate and continue in 2013, a number of ganetespib trials sponsored by third parties, including cooperative groups, foundations, and individual investigators, have recently been initiated or are expected to initiate in 2013.

Elesclomol (Mitochondria-Targeting Agent)

Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death (apoptosis), in cancer cells through a novel mechanism: disrupting cancer cell mitochondrial metabolism. In preclinical experiments, anti-cancer activity of elesclomol has been shown to correlate with certain biomarkers, including LDH, which can be associated with mitochondrial activity. When sufficient oxygen is present, the mitochondria generate cellular energy through processing oxygen, and there are low levels of LDH. When there is insufficient oxygen present, mitochondrial energy generation is reduced and there is increased reliance on glycolysis, which comes with increased levels of LDH. Consistent with these findings, in three randomized clinical trials, baseline LDH level was an important predictor of elesclomol treatment outcome.

Our current clinical program for elesclomol includes (1) a Phase 1 clinical trial of elesclomol as a monotherapy in acute myeloid leukemia (AML) being conducted at Princess Margaret Hospital in Toronto, Canada and at MSKCC in New York and (2) a Phase 2 clinical trial of elesclomol in combination with paclitaxel for the treatment of persistent or recurrent ovarian, fallopian tube or primary peritoneal cancer for patients with total baseline serum LDH level less than 0.8 times ULN being conducted by the Gynecological Oncology Group (GOG).

Hsp90-inhibitor Drug Conjugate (HDC) Platform

In September 2013, we announced the launch of a novel, proprietary small molecule cancer drug development program, the HDC Platform, which takes advantage of the tumor accumulation properties of Hsp90 inhibitors to increase the selective delivery to tumors of small molecule anti-cancer therapies. In October 2013 we announced the publication of the first key patent application covering our proprietary HDC technology, including composition of matter claims covering over 400 HDC compounds synthesized by us to date, methods for identifying therapeutically effective compounds, and methods of use against a wide range of diseases and conditions.

Small molecule inhibitors of Hsp90, including ganetespib as well as first-generation inhibitors such as 17-AAG and its derivatives, have been shown by our scientists and many other researchers to be retained in tumors for as much as 20 times longer than in blood or normal tissue. These properties are believed to be due to overexpression of an active form of Hsp90 in cancer cells as compared to normal tissues. Several groups have recently applied these results, by attaching a fluorescent probe to an Hsp90 inhibitor, as a novel means to image tumors in patients.

HDCs are drug candidates consisting of an Hsp90 inhibitor (targeting moiety) joined to an anti-cancer agent (payload) via a cleavable chemical linker optimized for controlled release of payload drug inside cancer cells. Because HDCs are small molecules, they diffuse into the cell passively, avoiding reliance on cell surface antigens or transporters, as is required by other delivery mechanisms such as antibody-drug conjugates (ADCs).

The longer retention of Hsp90 inhibitors in tumors results in higher concentration and longer duration of active payload drug inside cancer cells than occurs with standard administration of unconjugated chemotherapy or other payloads. This enhanced delivery creates the potential for greater cancer cell killing and reduced side effects.

Synta has developed over 400 HD-Conjugated chemotherapeutics, kinase inhibitors, hormone therapies, immunomodulators, and epigenetic modifiers, creating the potential for next-generation compounds in each of these categories. Examples include HD-Conjugated bendamustine, temozolomide, doxorubicin, 5-FU, pemetrexed, SN-38, topotecan, vorinostat, panobinostat, fulvestrant, abiraterone, lenalidomide, pomalidomide, docetaxel, carboplatin, bortezomib, sunitinib, and sorafenib.

Proof-of-concept has been established in preclinical models of cancer. HDC improved delivery of SN-38 anti-cancer payload, achieving over 30 times the concentration in tumor as compared to the concentration in plasma and other tissues. Strongly enhanced anti-tumor activity was seen with the HD-Conjugated SN-38

as compared to the unconjugated anti-cancer therapy in a broad range of animal models of cancer, including breast cancer, colon cancer, ovarian cancer, small cell lung cancer, bladder cancer, and melanoma.

STA-9584 (Vascular Disrupting Agent)

STA-9584 is a novel, injectable, small molecule compound that appears to disrupt the blood vessels that supply tumors with oxygen and essential nutrients, and is in preclinical development. In March 2011, we received a \$1 million grant from the United States Department of Defense (DoD) for the development of STA-9584 in advanced prostate cancer and initiated work on this study in the second quarter of 2011. We completed work covered by this grant in 2012.

Our Inflammatory Disease Programs

We have two preclinical-stage programs focusing on treatments for inflammatory diseases. Both of our inflammatory disease programs focus on oral, disease-modifying drug candidates that act through novel mechanisms and could potentially target multiple indications.

CRACM Ion Channel Inhibitors

We have developed novel, small molecule inhibitors of CRACM ion channels expressed on immune cells. Our CRACM ion channel inhibitors have shown anti-inflammatory activity in preclinical studies both *in vitro* and *in vivo*, inhibiting T cell and mast cell activity, including cytokine release, degranulation, and immune cell proliferation. Potential applications include a wide range of inflammatory diseases and disorders for which modulating T cell and mast cell function has been shown to be critical, including rheumatoid arthritis (RA), asthma, chronic obstructive pulmonary disease (COPD), allergy, transplant rejection, and other autoimmune diseases and inflammatory conditions. We have several CRACM inhibitors in preclinical development. Because there are a number of CRACM ion channel targets on immune cells, we believe that CRACM inhibitor compounds can be developed that target different diseases.

IL-12/23 Inhibitors

The IL-12 cytokine is an important "master switch" that triggers the immune response of the T cell known as T helper type 1 (Th1). T cells play a critical role in the coordination of the body's immune response, and while Th1 cells are normally involved in the body's defense against intracellular attack by bacteria and other microorganisms, an overactive Th1 response can lead to various autoimmune or inflammatory diseases including Crohn's disease, psoriasis, RA, multiple sclerosis, and common variable immunodeficiency. The IL-23 cytokine is critical to the generation of a class of T cells known as Th17, which produce other pro-inflammatory proteins such as IL-17, which are critical in driving chronic inflammation. We believe that the clinical trial results observed with anti-IL-12/23 antibody therapies validate the inhibition of IL-12/23 activity as a promising approach for the treatment of inflammatory and autoimmune diseases. We have identified several small molecule IL-12/23 inhibitors that represent an opportunity to develop drug candidates that could be administered orally and potentially address a wide range of serious inflammatory diseases with high unmet medical needs.

Company Strategy

Our strategy is to discover, develop, and commercialize novel small molecule drug candidates for treating severe medical conditions, including cancer and chronic inflammatory diseases, using our unique collection of assets, technologies, and capabilities in drug discovery and development. Important elements of our long-term strategy include:

- exploiting the unique, first-in-class/best-in-class potential of our existing drug candidates to establish and achieve sustainable advantages relative to other therapeutic options;
- using our translational research and biomarker identification capabilities, together with our collaborations with leading researchers and investigators, to identify the patient populations most likely to derive benefit from our drug candidates and using those findings to optimize our clinical trial choices;

- maintaining the flexibility to partner or retain individual programs, globally or regionally, to achieve creative and favorable partnership structures;
- maintaining a strong cash position, such that we have multiple options for continuing to advance our drug candidates either on our own or with a partner;
- using our discovery and development capabilities to expand and protect our intellectual property position for each of our programs; and
- using our proprietary compound library and discovery platform to continue to generate promising new drug candidates with distinct chemical structures, novel mechanisms of action, and broad therapeutic potential.

Corporate Information

Our principal executive offices are located at 45 Hartwell Avenue, Lexington, Massachusetts 02421, and our telephone number is (781) 274-8200. Our website address is www.syntapharma.com. The information contained on our website is not incorporated by reference into, and does not form any part of, this prospectus supplement or the accompanying prospectus. We have included our website address as a factual reference and do not intend it to be an active link to our website. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and all amendments to those reports, are available free of charge through the "Investors — SEC Filings" section of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC.

Our trademarks include, without limitation, Synta Pharmaceuticals, our corporate logo and the GALAXY Trial. Other service marks, trademarks and trade names contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and therein are the property of their respective owners.

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THE OFFERING

Common stock offered by us shares

Common stock to be outstanding after the offering shares (or shares if the underwriters' option to purchase additional shares is exercised in full)

Underwriters' Option to Purchase Additional Shares

We have granted the underwriters an option to purchase up to additional shares of our common stock. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.

Use of Proceeds

We intend to use the net proceeds of this offering for general corporate purposes, which may include research and development expenditures, clinical trial expenditures, manufacture and supply of drug substance and drug products, acquisitions of new technologies, capital expenditures and working capital. See the section entitled "Use of Proceeds" below.

NASDAQ Global Market Listing

Our common stock is listed on The NASDAQ Global Market under the symbol "SNTA."

Risk Factors

An investment in our common stock involves a high degree of risk. See the information contained in or incorporated by reference under "Risk Factors" beginning on page S-8 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

Outstanding Shares

The number of shares to be outstanding after this offering is based on 69,103,073 shares of common stock outstanding as of September 30, 2013. It does not include:

- 6,736,209 shares of our common stock issuable upon exercise of stock options outstanding as of September 30, 2013 under our stock option plans as of that date, at a weighted average exercise price of \$6.97 per share; and
- 1,628,225 shares of our common stock available as of September 30, 2013 for future grant or issuance pursuant to our stock-based plan for employees, directors and consultants.

Unless otherwise indicated, all information in this prospectus supplement assumes that the underwriters will not exercise the option to purchase additional shares granted to them by us.

Certain of our directors and officers and entities affiliated with these directors and officers have indicated an interest in purchasing shares of our common stock in this offering. However, because these indications of interest are not binding agreements or commitments to purchase, these directors, officers and entities may elect not to purchase any shares in this offering.

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, 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 operation 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 Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception, and we expect to incur losses for the foreseeable future and may never reach profitability.

Since inception we have incurred significant operating losses and, as of September 30, 2013, we had an accumulated deficit of \$527.3 million. We expect to continue to incur significant operating expenses and capital expenditures and anticipate that our expenses and losses may increase substantially in the foreseeable future as we:

- complete the ongoing clinical trials of ganetespib in solid tumors, including the GALAXY-1, GALAXY-2, ENCHANT-1 and CHIARA trials, and initiate additional clinical trials of ganetespib if supported by trial results;
- complete preclinical development of an additional Hsp90 inhibitor and initiate clinical trials of this compound, if supported by the preclinical data;
- complete the ongoing clinical trials of elesclomol in AML and ovarian cancers, and initiate additional clinical trials of elesclomol, if supported by trial results;
- complete preclinical development of STA-9584 and initiate clinical trials, if supported by preclinical data;
- advance our CRACM inhibitor into preclinical development and initiate clinical trials, if supported by preclinical data;
- advance our HDC program into preclinical development and initiate clinical trials, if supported by preclinical data;
- discover, develop, and seek regulatory approval for backups of our current drug candidates and other new drug candidates;
- identify additional compounds or drug candidates and acquire rights from third parties to those compounds or drug candidates through licenses, acquisitions or other means; and
- commercialize any approved drug candidates.

We must generate significant revenue to achieve and maintain profitability. Even if we succeed in developing and commercializing one or more of our drug candidates, we may not be able to generate sufficient revenue and we may never be able to achieve or maintain profitability.

If we fail to obtain the funding necessary to support our operations, we will be unable to successfully develop and commercialize our lead drug candidates.

Although we have raised substantial funding to date, we will require additional funding in order to complete clinical development and commercialize our current drug candidates and to conduct the research and development and clinical and regulatory activities necessary to bring any future drug candidates to market. Our future funding requirements will depend on many factors that are currently unknown to us, including:

- the progress and results of our ongoing clinical trials of ganetespib and elesclomol, and any additional clinical trials we may initiate in the future based on the results of these clinical trials;

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- the results of our preclinical studies of any additional Hsp90 inhibitors we may develop, our CRACM inhibitors, STA-9584 and our HDC program, and our decision to initiate clinical trials, if supported by the preclinical and other test results;
- uncertainty associated with costs, timing, and outcome of regulatory review of our drug candidates;
- the scope, progress, results, and cost of preclinical development, clinical trials, and regulatory review of any new drug candidates we may discover or acquire;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims;
- our ability to establish additional strategic collaborations and licensing or other arrangements on terms favorable to us
- the costs to satisfy our obligations under potential future collaborations; and
- the timing, receipt, and amount of sales or royalties, if any, from ganetespib, elesclomol, STA-9584, our CRACM inhibitors, our IL-12/23 inhibitors and our other potential products.

There can be no assurance that additional funds will be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available on a timely basis, we may be required to:

- terminate, significantly modify or delay our research and development programs;
- reduce our planned commercialization efforts; or
- obtain funds through collaborators that may require us to relinquish rights to our technologies or drug candidates that we might otherwise seek to develop or commercialize independently.

We do not anticipate that we will generate product revenue in the foreseeable future, if at all. We expect our continuing operations to use cash over the next several years and such cash use may increase significantly from year to year. While we are engaged in multiple preliminary partnership discussions for each of our currently unpartnered programs, including ganetespib, elesclomol, STA-9584, our CRACM inhibitors, our IL-12/23 inhibitors, and our HDC platform, which could result in one or more new partnership agreements that may include upfront payments and cost-sharing provisions, there is no guarantee we will be successful in entering into any such partnership agreements on commercially reasonable terms, if at all, or that we will receive any other revenue through these partnership efforts in the future. Based on our current operating levels, we expect our cash resources (excluding any proceeds we may receive from this offering) will be sufficient to fund operations into the second quarter of 2014. This estimate assumes that the timing and nature of activities contemplated for the remainder of 2013 and 2014 will be conducted subject to the availability of sufficient financial resources. We expect to continue to evaluate additional potential sources of funding, including partnership agreements, cost or risk-sharing arrangements, equity financings, use of our \$28 million at-the-market issuance sales agreement with MLV and other sources.

However, our operating plans may change as a result of many factors currently unknown to us, and we may need additional funds sooner than planned. In addition, we may seek additional capital due to favorable market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans.

Our operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.

We commenced operations in July 2001. Our operations to date have been limited to organizing and staffing our company, acquiring, developing, and securing our technology, and undertaking preclinical studies and clinical trials of our drug candidates. We have not yet demonstrated an ability to obtain regulatory approval, formulate and manufacture a commercial-scale product, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or had previously discovered, developed, and/or commercialized an approved product.

Raising additional capital may cause dilution to existing stockholders, restrict our operations or require us to relinquish rights.

We may seek the additional capital necessary to fund our operations through public or private equity offerings, collaboration agreements, debt financings, or licensing arrangements. To the extent that we raise additional capital through the sale of equity or convertible debt securities, existing stockholders' ownership interests will be diluted and the terms may include liquidation or other preferences that adversely affect their rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring additional debt, making capital expenditures, or declaring dividends. For example, the terms of our Loan and Security Agreement with General Electric Capital Corporation subject us to certain negative covenants including a prohibition on declaring or paying dividends. If we raise additional funds through collaboration and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or drug candidates, or grant licenses on terms that are not favorable to us.

Our existing loan and security agreements contain affirmative and negative covenants that may restrict our business and financing activities. If we fail to comply with covenants in our loan and security agreements, we may be required to repay our indebtedness thereunder, which may have an adverse effect on our liquidity.

On September 30, 2010, we entered into a \$15 million loan and security agreement with General Electric Capital Corporation, or GECC, and MidCap Funding III, LLC, which we refer to herein as the GECC Term Loan. In March 2013, we amended the GECC Term Loan, obtaining \$12.9 million in additional loan funding and, as a result, increasing the principal balance to \$22.5 million at March 31, 2013. We will make interest-only payments for the period of April 2013 through December 2013. Beginning in January 2014, we will begin making 30 equal monthly payments of principal plus accrued interest on the outstanding balance. The GECC Term Loan is secured by substantially all of our assets, except our intellectual property. We have, however, granted GECC a springing security interest in our intellectual property in the event that we are not in compliance with certain cash burn covenants set forth in the agreement. In addition, the GECC Term Loan contains restrictive covenants, including the requirement for us to receive prior written consent of GECC to enter into loans, other than up to \$4.0 million of equipment financing, restrictions on the declaration or payment of dividends, restrictions on acquisitions, and customary default provisions that include material adverse events, as defined therein. Our failure to comply with these covenants may result in the declaration of an event of default that, if not cured or waived, may result in the acceleration of the maturity of indebtedness outstanding under the GECC Term Loan, which would require us to pay all amounts outstanding. If an event of default occurs, we may not be able to cure it within any applicable cure period, if at all. If the maturity of our indebtedness is accelerated, we may not have sufficient funds available for repayment or we may not have the ability to borrow or obtain sufficient funds to replace the accelerated indebtedness on terms acceptable to us or at all.

In March 2011, we entered into a \$2 million loan and security agreement with Oxford Finance Corporation, or Oxford, which we refer to as the Oxford Term Loan. In December 2012, we entered into a loan modification agreement under which we may draw down up to an additional \$0.6 million in equipment financing until June 30, 2013, which has been fully utilized. The Oxford Term Loan is secured by certain laboratory and office equipment, furniture and fixtures. In connection with the Oxford Term Loan, Oxford and GECC entered into a Lien Subordination Agreement, whereby GECC granted Oxford a first priority perfected security interest in the Oxford loan collateral, including the fully utilized \$0.6 million. The Oxford Term Loan contains restrictive covenants, including the requirement for us to receive the prior written consent of Oxford to enter into acquisitions in which we incur more than \$2.0 million of related indebtedness, and customary default provisions that include material adverse events, as defined therein.

Risks Related to the Development and Regulatory Approval of Our Drug Candidates

Our success is largely dependent on the success of ganetespib, elesclomol and our other drug candidates, and we cannot be certain that we will be able to obtain regulatory approval for or successfully commercialize any of these drug candidates.

We anticipate that our success will depend largely on the receipt of regulatory approval and successful commercialization of our drug candidates: ganetespib, elesclomol, STA-9584, our preclinical-stage CRACM inhibitors and any HDC drug candidates we may develop. The future success of our drug candidates will depend on several factors, including the following:

- our ability to recruit appropriate patients into our clinical trials and to complete the necessary preclinical studies and clinical trials to support regulatory approval;
- our ability to provide acceptable evidence of their safety and efficacy;
- receipt of marketing approval from the U.S. Food and Drug Administration, or FDA, and any similar foreign regulatory authorities;
- obtaining and maintaining commercial manufacturing arrangements with third-party manufacturers or establishing commercial-scale manufacturing capabilities;
- in the case of elesclomol, a further understanding of the role of LDH levels and other potential markers of treatment outcome, and the outcome of our ongoing and contemplated clinical trials of elesclomol that we may initiate;
- establishing an internal sales force or collaborating with pharmaceutical companies or contract sales organizations to market and sell any approved drug;
- approval or use of competitive products in the indications for which we will market our drug candidates;
- validation of the molecular targets or mechanisms of action of our drug candidates by us or by third parties;
- approval of reimbursement in foreign countries with centralized health care; and
- acceptance of any approved drug in the medical community and by patients and third-party payors.

Many of these factors are beyond our control. Accordingly, there can be no assurance that we will ever be able to generate revenues through the sale of an approved product or through strategic collaborations based on our products.

If we do not obtain the required regulatory approvals, we will be unable to market and sell our drug candidates.

Our drug candidates are subject to extensive governmental regulations relating to development, clinical trials, manufacturing, and commercialization. Rigorous preclinical testing and clinical trials and an extensive regulatory review and approval process are required to be successfully completed in the United States and in many foreign jurisdictions before a new drug can be sold. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain, and subject to unanticipated delays. The time required to obtain approval by the FDA is unpredictable but typically exceeds five years following the commencement of clinical trials, depending upon the complexity of the drug candidate and the indication.

We have limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. In connection with the clinical trials of our drug candidates, we face risks that:

- the drug candidate may not prove to be safe and effective;
- the dosing of the drug candidate in a particular clinical trial may not be optimal;
- patients may die or suffer other adverse effects for reasons that may or may not be related to the drug candidate being tested;

- the results may not confirm the positive results of earlier clinical trials or preclinical studies; and
- the results may not meet the level of statistical significance or clinical benefit-to-risk ratio required by the FDA or other regulatory agencies for marketing approval.

Of the large number of drugs in development, only a small percentage result in the submission of a new drug application, or NDA, to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market a commercial product, any such approval may be subject to limitations on the indicated uses for which we may market the product.

In clinical studies with elesclomol, we have begun to use a new formulation. However, we have limited prior clinical experience with this formulation and cannot ensure that no new toxicities will be observed in current or future clinical trials with elesclomol.

Although the FDA has given us permission to resume clinical development of elesclomol following specific protocols that exclude patients with elevated LDH levels, we are using a different formulation of elesclomol than we used in our prior completed elesclomol clinical trials. The prior formulation utilized the free acid form of elesclomol, which needed to be dissolved in an organic solvent prior to administration. The types of combination therapies that were possible with the free acid formulation of elesclomol, and the amount of elesclomol that could be delivered safely in this formulation, were limited because of the additional toxicities caused by presence of the organic solvent. Accordingly, we have developed a water-soluble, lyophilized sodium salt form of elesclomol, or elesclomol sodium, that does not need to be dissolved in an organic solvent and therefore has the potential to be used more easily with other oncology products or as a stand alone agent without need for an organic solvent. We are using this formulation in current clinical trials of elesclomol and intend to continue using this formulation for future studies and for commercialization, if elesclomol is approved. Although we have shown comparable pharmacokinetics of the new formulation of lyophilized elesclomol sodium in animals, we can provide no guarantees that the sodium salt formulation will be commercially suitable, that efficacy will be established or that new toxicities or other adverse effects will not be identified in the clinical trials that we conduct with this formulation. In addition, we have noted a relatively high pH in the final elesclomol infusion solution. Although there have been no reported concerns in the ongoing clinical trials using this solution, we cannot guarantee that there will be no complications related to the high pH of this solution in the future.

If we are unable to successfully reformulate and scale up ganetespib, it may limit the commercial potential of this drug candidate, even if approved.

The current formulation and administration procedures for ganetespib may be inconvenient or unacceptable to certain patients due to the method of administration and frequency of dosing. These factors may lead to slower enrollment rates in our clinical trials and, if approved, may limit the commercial potential of ganetespib. In addition, to date, we have only produced ganetespib active pharmaceutical ingredient, or API, and drug product, or DP, on a relatively small scale. Our current plan is to increase the API and DP manufacturing scale by several fold relative to the current scale in the upcoming process validation batches and in future commercial batches. Although we believe that the current processes for producing ganetespib API and DP formulation are fully scalable, these products may prove to be unexpectedly challenging to manufacture on a larger, commercial scale, which may add to the cost of manufacture. While we have identified an improved formulation of ganetespib that we believe may broaden its commercial potential and decrease manufacturing risk, this new formulation is being tested in limited clinical trials. While we believe that bioequivalence between the improved and the first generation formulation has been demonstrated, we will continue to monitor the performance of the new formulation in the ongoing clinical studies. If the improved drug product formulation is not commercially acceptable and we are unable to develop a commercially acceptable formulation using our own know-how or technology, we may need to rely on third party proprietary formulation technology. Such third party formulation development may require significant time and expense. We cannot assure you that our efforts to reformulate ganetespib will be

successful. If we are unable to reformulate ganetespib, ganetespib may have more limited potential target indications and market size if it is approved.

While we believe that elesclomol's mechanism of action may have applicability to a broad range of solid tumor cancers, most of our clinical trials of elesclomol to date have shown negative or inconclusive results and there can be no assurances that future clinical trials of elesclomol will yield positive results.

Based on our understanding of the mechanism of action and the preclinical activity we have seen with elesclomol, we believe that elesclomol may have applicability to a broad range of cancers. However, other than our Phase 2b clinical trial in metastatic melanoma, the results of our clinical trials of elesclomol have been negative or inconclusive. We have completed Phase 2 clinical trials of elesclomol in sarcoma and non-small cell lung cancer. The results of the soft tissue sarcoma clinical trial did not definitively establish evidence of clinical activity. In the non-small cell lung cancer clinical trial, no improvement was observed in time-to-progression between combination treatment with elesclomol and a standard first-line combination therapy. In February 2009, we announced that we were suspending the SYMMETRY trial, our global, pivotal Phase 3 clinical trial of elesclomol for the treatment of metastatic melanoma. In subsequent analyses, although we identified a population of patients (those who did not have elevated levels of LDH) for which the primary endpoint of progression-free survival, or PFS, was achieved and the safety profile was acceptable, the SYMMETRY trial did not achieve the primary endpoint of the study and therefore will not support approval of elesclomol in metastatic melanoma. We have been analyzing data from these trials to assess the future development of elesclomol in melanoma and other cancer types and the FDA has given us approval to resume clinical development of elesclomol following specific protocols that exclude patients with elevated LDH levels. Although a Phase 2 trial of elesclomol in ovarian cancer and a Phase 1 trial in AML are ongoing, there can be no assurance that elesclomol will prove effective in and be approved for treating these or other forms of cancer.

Because our drug candidates are in an early stage of development, there is a high risk of failure, and we may never succeed in developing marketable products or generating product revenue.

We have no drug candidates that have received regulatory approval for commercial sale. We do not expect to have any commercial products on the market in the foreseeable future, if at all. We are exploring human diseases at the cellular level and attempting to develop drug candidates that intervene with cellular processes. Drug development is an uncertain process that involves trial and error, and we may fail at numerous stages along the way. Success in preclinical studies of a drug candidate may not be predictive of similar results in humans during clinical trials, and successful results from early or small clinical trials of a drug candidate may not be replicated in later and larger clinical trials. For example, although our Phase 2b clinical trial of elesclomol for the treatment of metastatic melanoma achieved the primary endpoint of increasing PFS, the SYMMETRY trial did not achieve the primary endpoint of PFS and therefore will not support approval of elesclomol in metastatic melanoma. Accordingly, the results from preclinical studies and the completed and ongoing clinical trials for our drug candidates may not be predictive of the results we may obtain in later stage clinical trials.

If clinical trials for our drug candidates are prolonged, delayed or suspended, we may be unable to commercialize our drug candidates on a timely basis, which would require us to incur additional costs and delay our receipt of any revenue from potential product sales.

We cannot predict whether we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our other ongoing and planned clinical trials and negatively impact our ability to obtain regulatory approval for, and to market and sell, a particular drug candidate, including our clinical drug candidates, ganetespib and elesclomol, and our drug candidates that are still in preclinical studies,

including STA-9584, our CRACM inhibitor candidates, our IL-12/23 inhibitor candidates and our HDC candidates:

- conditions imposed on us by the FDA or any foreign regulatory authority regarding the scope or design of our clinical trials;
- delays in obtaining, or our inability to obtain, required approvals from institutional review boards or other reviewing entities at clinical sites selected for participation in our clinical trials;
- insufficient supply or deficient quality of our drug candidates or other materials necessary to conduct our clinical trials;
- delays in obtaining regulatory agreement for the conduct of our clinical trials;
- lower or slower than anticipated enrollment and retention rate of subjects in clinical trials;
- negative or inconclusive results from clinical trials, or results that are inconsistent with earlier results, that necessitate additional clinical trials (for example, due to patient-to-patient pharmacokinetic variability);
- serious and unexpected drug-related side effects experienced by patients in clinical trials; or
- failure of our third-party contractors to comply with regulatory requirements or otherwise meet their contractual obligations to us.

Commercialization of our drug candidates may be delayed by the imposition of additional conditions on our clinical trials by the FDA or any foreign regulatory authority or the requirement of additional supportive studies by the FDA or any foreign regulatory authority. In addition, clinical trials require sufficient patient enrollment, which is a function of many factors, including the size of the target patient population, the nature of the trial protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, the conduct of other clinical trials that compete for the same patients as our clinical trials, and the eligibility criteria for our clinical trials. Our failure to enroll patients in our clinical trials could delay the completion of the clinical trial beyond our expectations. In addition, the FDA could require us to conduct clinical trials with a larger number of subjects than we have projected for any of our drug candidates. We may not be able to enroll a sufficient number of patients in a timely or cost-effective manner. Furthermore, enrolled patients may drop out of our clinical trials, which could impair the validity or statistical significance of the clinical trials.

We do not know whether our clinical trials will begin as planned, will need to be restructured, or will be completed on schedule, if at all. Delays in our clinical trials will result in increased development costs for our drug candidates. In addition, if our clinical trials are delayed, our competitors may be able to bring products to market before we do and the commercial viability of our drug candidates could be limited. If approved, we may not receive a package insert for any of our products that are competitive and differentiated, which may change our strategies with respect to how and when we commercialize any of our products.

Failure to comply with foreign regulatory requirements governing human clinical trials and marketing approval for drugs could prevent us from selling our drug candidates in foreign markets, which may adversely affect our operating results and financial condition.

The requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement for marketing our drug candidates outside the United States vary greatly from country to country and may require additional testing. We expect that our future clinical development of our drug candidates will involve a number of clinical trials in foreign jurisdictions, particularly in Europe. We have no experience in obtaining foreign regulatory approvals. The time required to obtain approvals outside the United States may differ from that required to obtain FDA approval. We may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not guarantee approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other countries or by the FDA. Failure to comply with these regulatory requirements or obtain required approvals

could impair our ability to develop foreign markets for our drug candidates and may have a material adverse effect on our results of operations and financial condition.

Our drug candidates will remain subject to ongoing regulatory review even if they receive marketing approval, and if we fail to comply with continuing regulations, we could lose these approvals and the sale of any approved commercial products could be suspended.

Even if we receive regulatory approval to market a particular drug candidate, the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion, and record keeping related to the product will remain subject to extensive regulatory requirements. If we fail to comply with the regulatory requirements of the FDA and other applicable domestic and foreign regulatory authorities or previously unknown problems with any approved commercial products, manufacturers, or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions, including:

- restrictions on the products, manufacturers, or manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- import bans;
- suspension or withdrawal of regulatory approvals;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new drug candidates or supplements to approved applications.

If side effects or toxicities increase or are identified during the time our drug candidates are in development or after they are approved and on the market, we may be required to perform lengthy additional clinical trials, change the labeling of any such products, or withdraw any such products from the market, any of which would hinder or preclude our ability to generate revenues.

We have observed significant toxicities in preclinical animal studies of our clinical drug candidate, ganetespib. In clinical trials to date, we have not observed the serious liver and common ocular toxicities observed with first generation Hsp90 inhibitors. However, if these or other serious toxicities occur at or below a clinical dose of ganetespib required to show efficacy, we may not be able to demonstrate that ganetespib is safe and effective. Even if we are successful in obtaining regulatory approval for one or more of our drug candidates, as the drug is used in a larger patient population, if the incidence of side effects or toxicities increases or if other unacceptable effects are identified:

- regulatory authorities may withdraw their approvals;
- we may be required to reformulate any such products, conduct additional clinical trials, make changes in labeling of any such products, or implement changes to or obtain new approvals of our or our contractors' manufacturing facilities;
- we may experience a significant drop in the sales of the affected products;
- our reputation in the marketplace may suffer; and
- we may become the target of lawsuits, including class action suits.

Any of these events could harm or prevent sales of the affected products or could substantially increase the costs and expenses of commercializing and marketing any such products.

While we choose to test our drug candidates in specific clinical indications based in part on our understanding of their mechanisms of action, our understanding may be incorrect or incomplete and, therefore, our drugs may not be effective against the diseases tested in our clinical trials.

Our rationale for selecting the particular therapeutic indications for each of our drug candidates is based in part on our understanding of the mechanism of action of these drug candidates. However, our understanding of the drug candidate's mechanism of action may be incomplete or incorrect, or the mechanism may not be clinically relevant to the diseases treated. In such cases, our drug candidates may prove to be ineffective in the clinical trials for treating those diseases.

We deal with hazardous materials and must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our activities involve the controlled storage, use, and disposal of hazardous materials, including cytotoxic agents, genotoxic agents, infectious agents, corrosive, explosive and flammable chemicals, and various radioactive compounds. We are subject to federal, state, and local laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. Although we believe that our safety procedures for the handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials.

In the event of an accident, state or federal authorities may curtail our use of these materials, and we could be liable for any civil damages that result, which may exceed our financial resources and may seriously harm our business. We currently maintain insurance covering hazardous waste cleanup costs in an amount of up to \$250,000 per site. Because we believe that our laboratory and materials handling policies and practices sufficiently mitigate the likelihood of materials liability or third-party claims, we currently carry no insurance covering such claims. While we believe that the amount of insurance we carry is sufficient for typical risks regarding our handling of these materials, it may not be sufficient to cover pollution conditions or other extraordinary or unanticipated events. Additionally, an accident could damage, or force us to shut down, our operations.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct our clinical trials and nonclinical safety assessment studies, and those third parties may not perform satisfactorily, including failing to meet established timelines for the completion of such clinical trials and studies.

We do not have the ability to independently conduct clinical trials and certain nonclinical safety assessment studies, particularly those studies conducted under Good Laboratory Practices, or GLP, for our drug candidates, and we rely on third parties such as contract research organizations, or CROs, medical institutions, and clinical investigators in the case of clinical trials, and CROs in the case of nonclinical safety assessment studies, to perform these functions. Our reliance on these third parties for clinical development activities reduces our control over these activities. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. To date, our CROs and other similar entities with which we are working have performed well; however, if these third parties do not successfully carry out their contractual duties, meet expected timelines, or comply with applicable regulatory requirements, we may be delayed in obtaining regulatory approvals for our drug candidates and may be delayed in our efforts to successfully commercialize our drug candidates for targeted diseases.

We have no manufacturing capacity and depend on third-party manufacturers to produce our clinical trial drug supplies.

We do not currently operate manufacturing facilities or testing facilities for clinical or commercial production of ganetespib or elesclomol, or any of our preclinical drug candidates. We have limited experience in drug manufacturing, and we lack the resources and the capabilities to manufacture any of our drug candidates on a clinical or commercial scale. As a result, we currently rely on third-party manufacturers to manufacture, test, release, supply, store, and distribute drug supplies for our clinical trials. Any performance failure on the part of our existing or future manufacturers could interrupt on-going clinical trials, delay clinical development or regulatory approval of our drug candidates or commercialization of any approved products, producing additional losses and depriving us of potential product revenue.

Our drug candidates require precise, high quality manufacturing. Failure by our contract manufacturers to achieve and maintain high manufacturing standards could result in patient injury or death, product recalls or withdrawals, delays or failures in testing or delivery, cost overruns, or other problems that could seriously hurt our business. Contract manufacturers may encounter difficulties involving production yields, quality control, and quality assurance. These manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state and foreign agencies to ensure strict compliance with current Good Manufacturing Practice regulations, or cGMPs, and other applicable U.S. and foreign government regulations and standards. We periodically audit our contract manufacturers responsible for supplying our clinical drug materials and have put quality agreements in place that we believe are appropriate for our materials. However, we do not have direct control over third party manufacturers' compliance with cGMPs and other standards and therefore, cannot provide assurance regarding such compliance.

If for some reason our contract manufacturers cannot perform as agreed, we may be unable to replace such third-party manufacturers in a timely manner and the production of our drug candidates would be interrupted, resulting in delays in clinical trials and additional costs. Switching manufacturers may be difficult because the number of potential manufacturers is limited and the FDA must approve any replacement manufacturer after our drug candidates are approved. Such approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our drug candidates after receipt of FDA approval. It may be difficult or impossible for us to find a replacement manufacturer on acceptable terms quickly, or at all.

We contract with single manufacturers for the production of elesclomol and ganetespib API and DP for clinical trials and the failure of these manufacturers to supply sufficient quantities of material on a timely basis could have a material adverse effect on our business.

We use single manufacturers for the supply of elesclomol and ganetespib: in each case, one for the synthesis of API and another for production of DP. The manufacturing processes for ganetespib API and DP are conventional and fully-scalable. We believe that the various steps of these processes can be accomplished by many possible third-party contract manufacturing organizations, or CMOs. We currently use multiple CMOs to manufacture the starting materials and reagents that we use to manufacture ganetespib, however we use a single CMO in the manufacturing of ganetespib API. We have screened other CMOs as potential back up manufacturers of API, and we believe that the manufacturing process for ganetespib API can effectively be transferred to one of these CMOs upon successful execution of technology transfer, process qualification, validation of test methods and compliance site inspections. We currently use a single CMO for manufacturing ganetespib DP that has specific experience in manufacturing oncology products and that has flexible scale manufacturing capabilities. We have screened other CMOs as additional potential back ups, and we believe that the manufacturing process for ganetespib API and DP can effectively be transferred to one of these CMOs upon successful execution of technology transfer, process qualification,

validation of test methods and compliance site inspections. We believe that the agreements we have entered into to date with our CMOs for ganetespib production are sufficient for our current requirements.

The manufacturing process for elesclomol API is conventional and fully-scalable. We believe that the various steps of this process can be accomplished by many possible third-party CMOs. We currently use a single CMO in the manufacturing of elesclomol API but we have a backup CMO that has previously manufactured elesclomol API on our behalf. The elesclomol sodium DP is lyophilized and manufactured under aseptic conditions. We believe that the process for manufacturing the elesclomol sodium DP is routine and can be performed by various different CMOs. We have entered into a contract with a CMO with specific experience in manufacturing oncology products and that has flexible scale manufacturing capabilities. We believe that the agreements to produce the elesclomol sodium DP that we have entered into to date would be sufficient for our anticipated requirements.

If any of these CMOs failed to perform under their contracts, we believe that we could readily transfer the manufacturing methods to other CMOs. However, there may be a significant time delay before we could secure the necessary materials and such a delay could have an adverse effect on our ability to conduct our clinical trials. In addition, we have not entered into any agreement with our CMOs for the supply of ganetespib or elesclomol on a commercial scale. There can be no assurance that we will be able to enter into such an agreement on favorable terms, if at all.

We anticipate continued reliance on third-party manufacturers if we are successful in obtaining marketing approval from the FDA and other regulatory agencies for any of our drug candidates.

To date, our drug candidates have been manufactured in relatively small quantities for preclinical testing and clinical trials by third-party manufacturers. If the FDA or other regulatory agencies approve any of our drug candidates for commercial sale, we expect that we would continue to rely, at least initially, on third-party manufacturers to produce commercial quantities of such approved drug candidates. These manufacturers may not be able to successfully increase the manufacturing capacity for any of our approved drug candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA or other regulatory authorities must review and approve. If our third-party manufacturers are unable to successfully increase the manufacturing capacity for a drug candidate, or we are unable to establish our own manufacturing capabilities, the commercial launch of any approved products may be delayed or there may be a shortage in supply.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our drug candidates, we may be unable to generate product revenue.

We do not currently have an organization for the sales, marketing, and distribution of pharmaceutical products. In order to commercialize and market any of our products that may be approved by the FDA, we must build our sales, marketing, managerial, and other non-technical capabilities or make arrangements with third parties to perform these services. If we are unable to establish adequate sales, marketing, and distribution capabilities, whether independently or with third parties, we may not be able to generate product revenue and we may not become profitable.

If we do not establish collaborations, we may have to alter our development plans.

Our drug development programs and potential commercialization of our drug candidates will require substantial additional cash to fund expenses. We own all rights to our two lead drug candidates, elesclomol and ganetespib, and are fully responsible for the associated development costs. Our strategy continues to include the potential of selectively collaborating with leading pharmaceutical and biotechnology companies to assist us in furthering development and potential commercialization of some of our drug candidates and research programs. We may enter into one or more of such collaborations in the future, especially for target indications in which the potential collaborator has particular therapeutic expertise or that involve a large, primary care market that must be served by large sales and marketing organizations or for markets outside

of North America. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on acceptable terms, or at all. Even if we successfully enter into a collaboration, we cannot provide assurance that our partner will perform its contractual obligations or will not terminate the agreement. If that were to occur, we may have to curtail the development of a particular drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of our sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring our drug candidates to market and generate product revenue.

Risks Related to Our Intellectual Property

If our patent position does not adequately protect our drug candidates or any future products, others could compete against us more directly, which would harm our business.

Our success depends in part on our ability to obtain and maintain proprietary protection for our drug candidates, technology, and know-how, to operate without infringing on the proprietary rights of others, and to prevent others from infringing our proprietary rights. Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology, inventions, and improvements that are important to the development of our business. We also rely on trade secrets, know-how, continuing technological innovation, and in-licensing opportunities, as appropriate, to develop and maintain our proprietary position.

We have also in-licensed various technologies to complement our ongoing clinical and research programs. These licenses generally extend for the term of the related patent and contain customary royalty, termination, and other provisions. We have a license agreement with Beth Israel Deaconess Medical Center that provides us with the exclusive commercial right to certain patent filings made by Beth Israel in the field of ion channels. We do not believe that this license agreement is currently material to our business. We also have a non-exclusive license to a U.S. patent assigned to Columbia University that could potentially cover a possible aspect of the elesclomol mechanism. This license is not royalty-bearing unless we include specific mechanism language on the label of any approved product, in which case a nominal royalty would be owed.

Our commercial success will depend in part on our ability to obtain additional patents and protect our existing patent position as well as our ability to maintain adequate protection of other intellectual property for our technologies, drug candidates, and any future products in the United States and other countries. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage we may have, which could harm our business and ability to achieve profitability. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, validity and enforceability cannot be predicted with certainty. Patents may be challenged, deemed unenforceable, invalidated, or circumvented. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our proprietary technologies, drug candidates, and any future products are covered by valid and enforceable patents or are effectively maintained as trade secrets.

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In addition, although we do not believe that any of the patents or patent applications that we currently license are material to our business, we may in the future license intellectual property that is material to us. In such cases, we may be dependent upon the licensors to obtain, maintain and enforce patent protection for the licensed intellectual property. These licensors may not successfully prosecute patent applications or may fail to maintain issued patents. The licensors may also determine not to pursue litigation against other companies that infringe the patents, or may pursue such litigation less aggressively than we would. If any of the foregoing occurs, and the terms of any such future license do not allow us to assume control of patent prosecution, maintenance and enforcement, any competitive advantage we may have due to the license may be diminished or eliminated.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- we or our licensors were the first to make the inventions covered by each of our pending patent applications;
- we or our licensors were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies;
- any of our or our licensors' pending patent applications will result in issued patents;
- any of our or our licensors' patents will be valid or enforceable;
- any patents issued to us or our licensors and collaborators will provide a basis for commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or drug candidates that are patentable; or
- the patents of others will not have an adverse effect on our business.

Although third parties may challenge our rights to, or the scope or validity of our patents, to date we have not received any communications from third parties challenging our patents or patent applications covering our drug candidates.

We typically file for patent protection first on the composition-of-matter of our drug candidates and also claim their activities and methods for their production and use to the extent known at that time. As we learn more about the mechanisms of action and new methods of manufacture and use of these drug candidates, we generally file additional patent applications for these new inventions. Although our patents may prevent others from making, using, or selling similar products, they do not ensure that we will not infringe the patent rights of third parties. For example, because we sometimes identify the mechanism of action or molecular target of a given drug candidate after identifying its composition-of-matter and therapeutic use, we may not be aware until the mechanism or target is further elucidated that a third party has an issued or pending patent claiming biological activities or targets that may cover our drug candidate. If such a patent exists or is granted in the future, we cannot provide assurances that a license will be available on commercially reasonable terms, or at all.

We may be unable to adequately prevent disclosure of trade secrets and other proprietary information.

We rely on trade secrets to protect our proprietary technologies, especially where we do not believe patent protection is appropriate or obtainable. However, trade secrets are difficult to protect. We rely in part on confidentiality agreements with our employees, consultants, outside scientific collaborators, sponsored researchers, and other advisors to protect our trade secrets and other proprietary information. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover our trade secrets and proprietary information. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Litigation or other proceedings or third-party claims of intellectual property infringement would require us to spend time and money and could prevent us from developing or commercializing our drug candidates.

Our commercial success will depend in part on not infringing upon the patents and proprietary rights of other parties and enforcing our own patents and proprietary rights against others. Certain of our research and development programs are in highly competitive fields in which numerous third parties have issued patents and patent applications with claims closely related to the subject matter of our programs. We are not currently aware of any litigation or other proceedings or claims by third parties that our drug candidates, technologies or methods infringe their intellectual property.

However, while it is our practice to conduct freedom to operate searches and analyses, we cannot guarantee that we have identified every patent or patent application that may be relevant to the research, development or commercialization of our drug candidates. In the case of patent applications, we assess the likelihood of claims in pending, third party patent applications being allowed which may interfere with our freedom to operate relative to our drug candidates. We cannot provide assurances that our assessments in this regard will be correct and that patent claims covering our drug candidates that were assessed a low likelihood of issuance by us will not issue to a third party in the future. Moreover, there can be no assurance that third parties will not assert against us patents that we believe are not infringed by us or are invalid. For example, we are aware of a U.S. patent that claims generic chemical structures, pharmaceutical formulations and methods of treatment relating to compounds similar to ganetespib and a U.S. patent that claims methods of treating certain cancers using Hsp90 inhibitors. We are also aware of an issued Japanese and European patent from the same family that claim generic chemical structures and compositions of matter relating to compounds similar to ganetespib. The claims of these patents may be relevant to the commercialization of our drug candidate, ganetespib. However, based on our analysis of these patents, we do not believe that the manufacture, use, importation or sale of ganetespib would infringe any valid claim of these patents. However, we cannot guarantee that these patents would not be asserted against us and, if asserted, that a court would find these patents to be invalid or not infringed.

In the event of a successful infringement action against us with respect to any third party patent rights, we may be required to:

- pay substantial damages;
- stop developing, commercializing, and selling the infringing drug candidates or approved products;
- stop utilizing the infringing technologies and methods in our drug candidates or approved products;
- develop non-infringing products, technologies, and methods; and
- obtain one or more licenses from other parties, which could result in our paying substantial royalties or our granting of cross licenses to our technologies.

We may not be able to obtain licenses from other parties at a reasonable cost, or at all. If we are not able to obtain necessary licenses at a reasonable cost, or at all, we could encounter substantial delays in product introductions while we attempt to develop alternative technologies, methods, and products, which we may not be able to accomplish.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is commonplace in our industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we have previously been subject to a claim by an alleged competitor that a prospective employee we sought to hire was bound by an ongoing non-competition obligation which prevented us from hiring this employee. We may be subject in the future to claims that our employees or prospective employees are subject to a continuing obligation to their former employers (such

as non-competition or non-solicitation obligations) or claims that our employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Risks Related to the Commercialization of Our Drug Candidates

If physicians and patients do not accept our future products or if the market for indications for which any drug candidate is approved is smaller than expected, we may be unable to generate significant revenue, if any.

Even if any of our current drug candidates or any other drug candidates we may develop or acquire in the future obtain regulatory approval, they may not gain market acceptance among physicians, healthcare payors, patients, and the medical community. Physicians may elect not to recommend these drugs for a variety of reasons including:

- timing of market introduction of competitive products;
- demonstration of clinical safety and efficacy compared to other products;
- cost-effectiveness;
- availability of reimbursement from government health programs and other third-party payors;
- convenience and ease of administration;
- prevalence and severity of adverse side effects;
- restrictions on the drug label;
- other potential advantages of alternative treatment methods; and
- ineffective marketing and distribution support of our products.

If any approved drugs fail to achieve market acceptance, we may not be able to generate significant revenue and our business would suffer.

If the government and third-party payors fail to provide coverage and adequate reimbursement rates for our future products, if any, our revenue and prospects for profitability will be harmed.

In both domestic and foreign markets, our sales of any future products will depend in part upon the availability of reimbursement from third-party payors. Such third-party payors include government health programs such as Medicare, commercial health insurers, and managed care organizations. These third-party payors are increasingly attempting to contain healthcare costs by demanding price discounts or rebates and limiting both coverage and the amounts that they will pay for new drugs, and, as a result, they may not cover or provide adequate payment for our drugs. We might need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to such payors' satisfaction. Such studies might require us to commit a significant amount of financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

U.S. and foreign governments continue to propose and pass legislation designed to reduce the cost of healthcare. For example, in some foreign markets, the government controls the pricing of prescription drugs. In the United States, we expect that there will continue to be federal and state proposals to implement similar governmental controls. In addition, Medicare and increasing emphasis on managed care in the United States will continue to put pressure on pharmaceutical product pricing. Cost control initiatives could decrease the price that we would receive for any products in the future, which would limit our revenue and profitability. Accordingly, legislation and regulations affecting the pricing of pharmaceuticals might change before our drug candidates are approved for marketing. Adoption of such legislation could further limit reimbursement for pharmaceuticals.

For example, the Medicare Prescription Drug Improvement and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drugs prescribed for the elderly and disabled and introduced new reimbursement methodologies. Although we do not know what the full impact of the new reimbursement methodologies will have on the prices of new drugs, we expect that there will be added pressure to contain and reduce costs. These cost reduction initiatives and other provisions of this legislation could decrease the coverage and price that we receive for any approved products, not only from Medicare, but also from private payors which often follow Medicare's policies, and could seriously harm our business.

Changes in healthcare policy could increase our costs, decrease our revenues and impact sales of and reimbursement for any approved products.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear how such a result could be avoided and what if any effect the research will have on the sales of our drug candidates, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our drug candidates. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

In March 2010, the President signed the Patient Protection and Affordable Care Act as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the ACA). The ACA is expected to have a significant impact on the health care industry. The ACA is expected to expand coverage for the uninsured while at the same time contain overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA is expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare D program. We cannot predict the impact of the ACA on pharmaceutical companies as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions which has not yet occurred. In addition, the current legal challenges to the ACA, as well as congressional efforts to repeal the ACA, add to the uncertainty of the legislative changes enacted as part of the ACA.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products.

If a successful product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, we could be forced to pay substantial damage awards.

The use of any of our drug candidates in clinical trials, and the sale of any approved products, might expose us to product liability claims. We currently maintain product liability insurance, and we monitor the amount of coverage we maintain as the size and design of our clinical trials evolve and adjust the amount of coverage we maintain accordingly. However, there can be no assurance that such insurance coverage will fully protect us against some or all of the claims to which we might become subject. We might not be able to maintain adequate insurance coverage at a reasonable cost or in sufficient amounts or scope to protect

us against potential losses. In the event a claim is brought against us, we might be required to pay legal and other expenses to defend the claim, as well as uncovered damages awards resulting from a claim brought successfully against us. Furthermore, whether or not we are ultimately successful in defending any such claims, we might be required to direct financial and managerial resources to such defense and adverse publicity could result, all of which could harm our business.

If we inadvertently violate the guidelines pertaining to promotion and advertising of our clinical candidates or approved products, we may be subject to disciplinary action by the FDA's Office of Prescription Drug Promotion or other regulatory bodies.

The FDA's Office of Prescription Drug Promotion or OPDP, formerly the Division of Drug Marketing, Advertising, and Communications, is responsible for reviewing prescription drug advertising and promotional labeling to ensure that the information contained in these materials is not false or misleading. There are specific disclosure requirements and the applicable regulations mandate that advertisements cannot be false or misleading or omit material facts about the product. Prescription drug promotional materials must present a fair balance between the drug's effectiveness and the risks associated with its use. Most warning letters from OPDP cite inadequate disclosure of risk information.

OPDP prioritizes its actions based on the degree of risk to the public health, and often focuses on newly introduced drugs and those associated with significant health risks. There are two types of letters that OPDP typically sends to companies which violate its drug advertising and promotional guidelines: notice of violation letters, or untitled letters, and warning letters. In the case of an untitled letter, OPDP typically alerts the drug company of the violation and issues a directive to refrain from future violations, but does not typically demand other corrective action. A warning letter is typically issued in cases that are more serious or where the company is a repeat offender. Although we have not received any such letters from OPDP, we may inadvertently violate OPDP's guidelines in the future and be subject to an OPDP untitled letter or warning letter, which may have a negative impact on our business.

We may be subject to federal and state laws prohibiting "kickbacks" and false or fraudulent claims, and federal and state physician payment disclosure laws which, if violated, could subject us to substantial penalties. Additionally, any challenge to or investigation into our practices under these laws could cause adverse publicity and be costly to respond to, and thus could harm our business.

A federal law commonly known as the federal anti-kickback law, and similar state laws, prohibit the payment of any remuneration that is intended to induce physicians or others either to refer patients or to acquire or arrange for or recommend the acquisition of health care products or services that are payable by Medicare, Medicaid and other federal health care programs. Other federal and state laws generally prohibit individuals or entities from knowingly presenting, or causing to be presented, claims for payment to federal health care programs such as Medicare and Medicaid or other third-party payors that are false or fraudulent, or for items or services that were not provided as claimed.

As part of the federal health care reform law, Congress enacted the Physician Payments Sunshine Act which will require applicable pharmaceutical and medical device manufacturers to monitor and report payments, gifts and other remuneration made to physicians and other health care professional and health care organizations. A number of states have enacted similar laws. Some state statutes, such as the one in Massachusetts, impose an outright ban on gifts to physicians. These laws are often referred to as "gift ban" or "aggregate spend" laws, and they carry substantial fines if they are violated.

In the event that we are found to have violated these laws or decide to settle a claim that we have done so, our business may be materially adversely affected as a result of any payments required to be made, restrictions on our future operations or actions required to be taken, damage to our business reputation or adverse publicity in connection with such a finding or settlement or other adverse effects relating thereto.

Additionally, even an unsuccessful challenge or investigation into our practices could cause adverse publicity, and be costly to respond to, and thus could harm our business and results of operations.

Risks Related to Our Industry

We may not be able to keep up with the rapid technological change in the biotechnology and pharmaceutical industries, which could make any future approved products obsolete and reduce our revenue.

Biotechnology and related pharmaceutical technologies have undergone and continue to be subject to rapid and significant change. Our future will depend in large part on our ability to maintain a competitive position with respect to these technologies. Our competitors may render our technologies obsolete by advances in existing technological approaches or the development of new or different approaches, potentially eliminating the advantages in our drug discovery process that we believe we derive from our research approach and proprietary technologies. In addition, any future products that we develop, including our clinical drug candidates, may become obsolete before we recover expenses incurred in developing those products, which may require that we raise additional funds to continue our operations.

Our market is subject to intense competition. If we are unable to compete effectively, our drug candidates may be rendered noncompetitive or obsolete.

We are engaged in segments of the pharmaceutical industry that are highly competitive and rapidly changing. Many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies, and other public and private research organizations are pursuing the development of novel drugs that target cancer and chronic inflammatory diseases. We face, and expect to continue to face, intense and increasing competition as new products enter the market and advanced technologies become available. In addition to currently approved drugs, there are a significant number of drugs that are currently under development and may become available in the future for the treatment of cancer and chronic inflammatory diseases. We would expect our drug candidates to compete with marketed drugs and potentially with drug candidates currently under development. Many of our competitors have:

- significantly greater financial, technical and human resources than we have and may be better equipped to discover, develop, manufacture and commercialize drug candidates;
- more extensive experience in preclinical testing and clinical trials, obtaining regulatory approvals and manufacturing and marketing pharmaceutical products;
- drug candidates that have been approved or are in late-stage clinical development; and/or
- collaborative arrangements in our target markets with leading companies and research institutions.

Competitive products may render our products obsolete or noncompetitive before we can recover the expenses of developing and commercializing our drug candidates. Furthermore, the development of new treatment methods and/or the widespread adoption or increased utilization of any vaccine for the diseases we are targeting could render our drug candidates noncompetitive, obsolete or uneconomical. If we successfully develop and obtain approval for our drug candidates, we will face competition based on the safety and effectiveness of our drug candidates, the timing of their entry into the market in relation to competitive products in development, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent position and other factors. If we successfully develop drug candidates but those drug candidates do not achieve and maintain market acceptance, our business will not be successful.

In particular, we believe that our products face the following sources of significant competition:

Ganetespiib. If approved, ganetespiib may compete against the currently approved therapies for the treatment of various cancer types and other cancer treatments currently under development. In particular, ganetespiib may compete with other agents under development that inhibit Hsp90, including retaspimycin

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hydrochloride (IPI-504), being developed by Infinity Pharmaceuticals, AU922, KW-2478, being developed by Kyowa Hakko Kirin, AT13387, being developed by Astex Pharmaceuticals, Debio0932, being developed by Curis/Debiopharma, DS-2248, being developed by Daiichi Sankyo, SNX-5422, being developed by Esanex, and PU-H71, being developed by Samus Therapeutics, among others.

Elesclomol. If approved, elesclomol may compete with the currently approved therapies for the treatment of cancers, and other cancer treatments currently under development. In particular, elesclomol may compete with other agents including but not limited to: a) agents whose mechanisms may involve the induction of oxidative stress including arsenic trioxide and hydroxyurea, among others; b) other mitochondria targeting agents and approaches for the selective delivery of anticancer agents to tumor cell mitochondria; and c) other modulators of cancer metabolism.

STA-9584. If approved, STA-9584 may compete with the currently approved therapies for the treatment of cancers, and other cancer treatments currently under development, including other vascular disrupting agents such as ZYBRESTAT and OXi4503, being developed by OXiGENE; AVE8062 (ombrabulin), being developed by Sanofi, BNC105, being developed by Bionomics, EPC-2407 (crolibulin), being developed by EpiCept, and NPI-2358 (plinabulin) being developed by Nereus Pharmaceuticals.

CRACM Ion Channel Inhibitors. If approved, CRACM inhibitors may compete with the currently approved therapies for the treatment of inflammatory diseases, and other anti-inflammatory treatments currently under development, including other CRACM inhibitors, oral inhibitors of other targets, and biologics approaches.

IL-12/23 Inhibitors. If approved, IL-12/23 inhibitors may compete against the currently approved therapies for the treatment of chronic inflammatory diseases, including:

- Stelara, a fully human monoclonal antibody targeting the p40 subunit of IL-12 and IL-23, marketed by Johnson & Johnson and approved in the U.S. and Europe for the treatment of plaque psoriasis and in Japan for the treatment of plaque psoriasis and psoriatic arthritis. IL-12/23 inhibitors may also compete with briakinumab (ABT-874), a fully human anti-IL-12/23 monoclonal antibody being developed by Abbott Laboratories. Regulatory applications in the U.S. and Europe for approval of briakinumab for the treatment of psoriasis were withdrawn in January 2011 following regulatory feedback indicating that further data and analysis would be required.
- large-molecule, injectable TNF-antagonists, including, among others: Remicade, marketed by Johnson & Johnson; Enbrel, marketed by Amgen and Wyeth Pharmaceuticals; and Humira, marketed by Abbott Laboratories; and
- broadly immunosuppressive small molecule agents including corticosteroids and azathioprine.

Hsp90-inhibitor Drug Conjugate Therapies. If approved, HDC therapies may compete with approved products that are designed to increase tumor exposure to an anticancer agent while sparing healthy tissues. These include Abraxane (paclitaxel protein-bound particles for injectable suspension), marketed by Celgene, Adcetris (brentuximab vedotin), marketed by Seattle Genetics, and Kadcyla (trastuzumab emtansine / T-DM1) marketed by Genentech. HDC therapies may also compete with other agents under development with the same objective of concentrating anticancer therapy in tumors using a variety of approaches. These include BIND-014, being developed by Bind Therapeutics, CDX-011, being developed by Celldex Therapeutics, Cobraxane, being developed by Access Pharmaceuticals, CRLX101, being developed by Cerulean, MM-398 and MM-302, being developed by Merrimack Pharmaceuticals, Opaxio, being developed by Cell Therapeutics, PEG-SN38 being developed by Enzon, PSMA-ADC, being developed by Progenics, VB4-845 and VB6-845, being developed by Viventia, vintafolide, being developed by Endocyte, XMT-1101 and XMT-1107 being developed by Mersana as well as other antibody drug conjugate candidate compounds in the pipelines of Immunogen, Seattle Genetics and their partners.

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Our ability to compete successfully will depend largely on our ability to leverage our experience in drug discovery, development and commercialization to:

- discover and develop medicines that are superior to other products in the market;
- attract high-quality scientific, product development, and commercial personnel;
- obtain patent and/or proprietary protection for our medicines and technologies;
- obtain required regulatory approvals;
- selectively commercialize certain drug candidates in indications treated by specialist physicians; and
- selectively partner with pharmaceutical companies in the development and commercialization of certain drug candidates.

Risks Related to Employee Matters and Managing Growth

We may be unsuccessful in retaining certain key personnel.

The competition for qualified personnel in the biotechnology field is intense and we must retain and motivate highly qualified scientific personnel. We are highly dependent on certain officers and employees, including Safi R. Bahcall, Ph.D., our President and Chief Executive Officer, and certain principal members of our executive and scientific teams. All of the agreements with these principal members of our executive and scientific teams provide that employment is at-will and may be terminated by the employee at any time and without notice. The loss of the services of any of these persons might impede the achievement of our research, development, and commercialization objectives. Recruiting and retaining qualified scientific personnel and possibly sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific personnel from universities and research institutions. We do not maintain "key person" insurance on any of our employees. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

If we make strategic acquisitions, we will incur a variety of costs and might never realize the anticipated benefits.

We have very limited experience in independently identifying acquisition candidates and integrating the operations of truly independent acquisition candidates with our company. Currently we are not a party to any acquisition agreements, nor do we have any understanding or commitment with respect to any such acquisition. If appropriate opportunities become available, however, we might attempt to acquire approved products, additional drug candidates, or businesses that we believe are a strategic fit with our business. If we pursue any transaction of that sort, the process of negotiating the acquisition and integrating an acquired product, drug candidate, or business might result in operating difficulties and expenditures and might require significant management attention that would otherwise be available for ongoing development of our business, whether or not any such transaction is ever consummated. Moreover, we might never realize the anticipated benefits of any acquisition. Future acquisitions could result in potentially dilutive issuances of equity securities, the incurrence of debt, contingent liabilities, or impairment expenses related to goodwill, and impairment or amortization expenses related to other intangible assets, which could harm our financial condition.

Risks Related to Our Common Stock

Our stock price has been and is likely to continue to be volatile and the market price of our common stock may drop.

Prior to our February 2007 initial public offering, there was not a public market for our common stock. There is a limited history on which to gauge the volatility of our stock price; however, since our common stock began trading on The NASDAQ Global Market on February 6, 2007 through September 30, 2013, our stock price has fluctuated from a low of \$1.20 to a high of \$11.88. Furthermore, the stock market has recently experienced significant volatility, particularly with respect to pharmaceutical, biotechnology, and other life sciences company stocks. The volatility of pharmaceutical, biotechnology, and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. Some of the factors that may cause the market price of our common stock to fluctuate include:

- results of our ongoing and contemplated clinical trials of ganetespib, and results from any other future clinical trials of ganetespib;
- results of our ongoing and contemplated clinical trials of elesclomol, and results from any other future clinical trials of elesclomol;
- results of clinical trials conducted by others on drugs that would compete with our drug candidates;
- failure or delays in advancing STA-9584, our preclinical-stage CRACM inhibitors, any HDC drug candidates we may develop, or other drug candidates we may discover or acquire in the future, into clinical trials;
- failure or discontinuation of any of our research programs;
- potential for merger or acquisition;
- key personnel changes;
- issues in manufacturing our drug candidates or approved products;
- regulatory developments or enforcement in the United States and foreign countries;
- developments or disputes concerning patents or other proprietary rights;
- introduction of technological innovations or new commercial products by us or our competitors;
- failure to secure adequate capital to fund our operations, or the issuance of equity securities at prices below fair market price;
- changes in estimates or recommendations by securities analysts, if any cover our common stock;
- public concern over our drug candidates or any approved products;
- litigation;
- future sales of our common stock and debt financing;
- general market conditions;
- changes in the structure of healthcare payment systems;
- failure of any of our drug candidates, if approved, to achieve commercial success;
- economic and other external factors or other disasters or crises;
- period-to-period fluctuations in our financial results; and
- overall fluctuations in U.S. equity markets.

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

Insiders have substantial control over us which could delay or prevent a change in corporate control or result in the entrenchment of management and/or the board of directors.

Prior to this offering, our directors and executive officers, together with their affiliates and related persons, beneficially own, in the aggregate, approximately 44.9% of our outstanding common stock. These stockholders, if acting together, may have the ability to determine the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation, or sale of all or substantially all of our assets. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our common stock by:

- delaying, deferring, or preventing a change in control;
- entrenching our management and/or the board of directors;
- impeding a merger, consolidation, takeover, or other business combination involving us; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

Provisions of our charter, bylaws, and Delaware law may make an acquisition of us or a change in our management more difficult.

Certain provisions of our restated certificate of incorporation and restated bylaws could discourage, delay, or prevent a merger, acquisition, or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. Stockholders who wish to participate in these transactions may not have the opportunity to do so. Furthermore, these provisions could prevent or frustrate attempts by our stockholders to replace or remove our management. These provisions:

- allow the authorized number of directors to be changed only by resolution of our board of directors;
- establish a classified board of directors, providing that not all members of the board of directors be elected at one time;
- authorize our board of directors to issue without stockholder approval blank check preferred stock that, if issued, could operate as a "poison pill" to dilute the stock ownership of a potential hostile acquirer to prevent an acquisition that is not approved by our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit stockholder action by written consent;
- establish advance notice requirements for stockholder nominations to our board of directors or for stockholder proposals that can be acted on at stockholder meetings;
- limit who may call stockholder meetings; and
- require the approval of the holders of 80% of the outstanding shares of our capital stock entitled to vote in order to amend certain provisions of our restated certificate of incorporation and restated bylaws.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may, unless certain criteria are met, prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a prescribed period of time.

Investors in this offering will pay a much higher price than the book value of our stock.

If you purchase common stock in this offering, you will incur an immediate and substantial dilution in net tangible book value of \$ _____ per share, after giving effect to the sale by us of _____ shares in this offering at the public offering price of \$ _____ per share. In addition, in the past, we have issued options to acquire common stock at prices below the offering price. To the extent these outstanding options are ultimately exercised, you will incur additional dilution. See the section entitled "Dilution" below for a more detailed discussion of the dilution you will incur in connection with this offering.

Our management will have broad discretion over the use of the net proceeds from this offering, and you may not agree with how we use the proceeds and the proceeds may not be invested successfully.

Our management will have broad discretion as to the use of the net proceeds from any offering by us and could use them for purposes other than those contemplated at the time of this offering. Accordingly, you may be relying on the judgment of our management with regard to the use of these net proceeds, and you will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. It is possible that the proceeds will be invested in a way that does not yield a favorable, or any, return for Synta.

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public markets could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We, our directors and our executive officers have agreed not to sell, dispose of or hedge any common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of this prospectus supplement continuing through and including the date 90 days after the date of this prospectus supplement, subject to certain exceptions. The underwriters may, in their discretion, release the restrictions on any such shares at any time without notice. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

We do not anticipate paying cash dividends, and accordingly, our stockholders must rely on stock appreciation for any return on their investment.

We currently intend to retain our future earnings, if any, to fund the development and growth of our business. In addition, we are currently prohibited from making a dividend payment under the terms of our loan and security agreement with General Electric Capital Corporation and MidCap Funding III, LLC. As a result, capital appreciation, if any, of our common stock will be the sole source of gain on an investment in our common stock for the foreseeable future.

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:

- the safety and efficacy of our product candidates;
- the timing, development and progress of our clinical and preclinical programs (including the timing of results of our ongoing trials and initiation of additional trials for ganetespib);
- our estimated expenditures and projected cash needs, including the sufficiency of cash resources (excluding the proceeds of this offering) to fund operations into the second quarter of 2014; and
- the use of proceeds from this offering.

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-8 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. 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 we will receive from this offering, based on the public offering price of \$ per share, will be approximately \$ million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, or approximately \$ million if the underwriters exercise their option to purchase additional shares in full.

We intend to use the net proceeds from this offering for general corporate purposes, which may include research and development expenditures, clinical trial expenditures, manufacture and supply of drug substance and drug products, acquisitions of new technologies, capital expenditures and working capital.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds from this offering. We have no current plans, commitments or agreements with respect to any acquisitions and may not make any acquisitions. Pending application of the net proceeds as described above, we intend to invest the net proceeds of the offering in short-term, investment-grade, interest-bearing securities.

DILUTION

If you purchase our common stock in this offering, your interest will be diluted to the extent of the difference between the public offering price per share and the net tangible book value per share of our common stock after this offering. We calculate net tangible book value per share by subtracting our total liabilities from our total tangible assets and dividing the difference by the number of outstanding shares of our common stock.

Our net tangible book value at September 30, 2013 was \$14.6 million, or \$0.21 per share. After giving effect to the sale of _____ shares of common stock by us at the public offering price of \$ _____ per share, less the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value at September 30, 2013 would be \$ _____ million, or \$ _____ per share. This represents an immediate increase in the as adjusted net tangible book value of \$ _____ per share to existing stockholders and an immediate dilution of \$ _____ per share to investors in this offering. The following table illustrates this per share dilution:

Public offering price per share	\$ _____
Net tangible book value per share as of September 30, 2013	\$ 0.21 _____
Increase per share attributable to this offering	_____
As adjusted net tangible book value per share after this offering	_____
Dilution per share to new investors	\$ _____

If the underwriters exercise their option to purchase additional shares in full, the as adjusted net tangible book value would increase to approximately \$ _____ million, or \$ _____ per share, representing an increase to existing stockholders of approximately \$ _____ per share, and there would be an immediate dilution of approximately \$ _____ per share to new investors.

The information above does not include:

- 6,736,209 shares of our common stock issuable upon exercise of stock options outstanding as of September 30, 2013 under our stock option plans as of that date, at a weighted average exercise price of \$6.97 per share; and
- 1,628,225 shares of our common stock available as of September 30, 2013 for future grant or issuance pursuant to our stock-based plan for employees, directors and consultants.

PRICE RANGE OF COMMON STOCK

Our common stock is listed on The NASDAQ Global Market under the symbol "SNTA." The last reported sale price for our common stock on November 11, 2013 was \$4.05 per share. The table below sets forth closing information on the range of high and low sales prices for our common stock during the periods indicated.

	High	Low
Fiscal Year ended December 31, 2011		
First Quarter	\$ 6.93	\$ 4.26
Second Quarter	6.27	4.30
Third Quarter	5.23	3.25
Fourth Quarter	5.15	3.02
Fiscal Year ended December 31, 2012		
First Quarter	\$ 5.74	\$ 4.03
Second Quarter	8.50	3.57
Third Quarter	8.54	5.35
Fourth Quarter	9.85	6.53
Fiscal Year ending December 31, 2013		
First Quarter	\$ 11.88	\$ 7.77
Second Quarter	10.74	3.76
Third Quarter	7.85	4.81
Fourth Quarter (through November 11, 2013)	7.10	3.88

DIVIDEND POLICY

We have never paid or declared any cash dividends on our common stock and we are currently prohibited from making any dividend payment under the terms of our loan and security agreement with General Electric Capital Corporation and MidCap Funding III, LLC. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, contractual restrictions, capital requirements, and other factors that our board of directors deems relevant.

UNDERWRITING

Subject to the terms and conditions set forth in the underwriting agreement, dated November , 2013, between us and Jefferies LLC, as the representative of the underwriters named below and the sole book-running manager of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

Underwriter	Number of Shares
Jefferies LLC	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the initial public offering price set forth on the cover page of this prospectus supplement and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ per share of common stock. The underwriters may allow, and certain dealers may reallow, a discount from the concession not in excess of \$ per share of common stock to certain brokers and dealers. After the offering, the initial public offering price, concession and reallowance to dealers may be reduced by the representative. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such

amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Per Share		Total	
	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions paid by us	\$	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$. We have agreed to reimburse the underwriters a maximum of \$20,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering. The underwriters have also agreed to reimburse us for certain of our expenses.

Listing

Our common stock is listed on The NASDAQ Global Market under the trading symbol "SNTA".

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus.

No Sales of Similar Securities

We and our officers and directors have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or
- otherwise dispose of any common shares, options or warrants to acquire common shares, or securities exchangeable or exercisable for or convertible into common shares currently or hereafter owned either of record or beneficially, or
- publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of Jefferies LLC.

This restriction terminates 90 days after the date of this prospectus supplement. However, subject to certain exceptions, in the event that either:

- during the last 17 days of the 90-day restricted period, we issue an earnings release or material news or a material event relating to us occurs, or
- prior to the expiration of the 90-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 90-day restricted period,

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then in either case the expiration of the 90-day restricted period will be extended until the expiration of the 18-day period beginning on the date of the issuance of an earnings release or the occurrence of the material news or event, as applicable, unless Jefferies LLC waives, in writing, such an extension.

Jefferies LLC may, in its sole discretion and at any time or from time to time before the termination of the 90-day period, without public notice, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that they, pursuant to Regulation M under the Securities Exchange Act of 1934, as amended, and certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

"Naked" short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on The NASDAQ Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the

highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriter and certain of its affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriter and certain of its affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriter and certain of its affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

NOTICE TO INVESTORS

Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia, or Corporations Act, has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company 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; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

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

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive, each referred to herein as a Relevant Member State, with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, referred to herein as the Relevant Implementation Date, no offer of any securities which are the subject of the offering contemplated by this prospectus has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the relevant competent authority in that Relevant Member State in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

- 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 representatives of the underwriters for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure

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implementing the Prospectus Directive in that Relevant 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 and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Hong Kong

No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or 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 of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended), or FIEL, and the Initial Purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been and will not be lodged or registered with the Monetary Authority of Singapore.

Accordingly, this prospectus and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public 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 as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

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Where the securities 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 under 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 is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

- to an institutional investor 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 \$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 given for the transfer; or
- where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, or FINMA, and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended, referred to herein as the Order, and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated. Each such person is referred to herein as a Relevant Person.

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other 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.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts. Covington & Burling LLP, New York, New York is counsel to the underwriters in connection with this offering.

EXPERTS

The consolidated financial statements of Synta Pharmaceuticals Corp. appearing in its Annual Report (Form 10-K) for the year ended December 31, 2012, and the effectiveness of Synta's internal control over financial reporting as of December 31, 2012 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting 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 may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's website at <http://www.sec.gov>.

This prospectus supplement and the accompanying prospectus are only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act of 1933, as amended, and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus supplement, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits and schedules, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

We also maintain a website at www.syntapharma.com, through which you can access our SEC filings. The information set forth on our website is not part of this prospectus supplement.

INCORPORATION OF DOCUMENTS 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 in this prospectus supplement by referring to those documents. The information incorporated by reference is considered to be part of this prospectus supplement, and information that we file, rather than furnish, later with the SEC will automatically update and supersede the information in this prospectus supplement. We incorporate by reference the following documents (unless otherwise noted, the SEC file number for each of the documents listed below is 001-33277):

- our Annual Report on Form 10-K, for the fiscal year ended December 31, 2012, filed with the SEC on March 14, 2013;
- our Quarterly Report on Form 10-Q, for the quarter ended March 31, 2013, filed with the SEC on April 30, 2013;
- our Quarterly Report on Form 10-Q, for the quarter ended June 30, 2013, filed with the SEC on August 1, 2013;
- our Quarterly Report on Form 10-Q, for the quarter ended September 30, 2013, filed with the SEC on November 4, 2013;
- our Current Reports on Form 8-K filed on March 8, 2013, March 13, 2013, April 1, 2013, May 6, 2013, June 3, 2013, June 17, 2013, July 29, 2013 (only the portions of Items 8.01 and 9.01 deemed to be "filed"), September 11, 2013, September 16, 2013 and October 30, 2013;
- the portions of our Definitive Proxy Statement on Schedule 14A that are deemed "filed" with the SEC under the Securities Exchange Act of 1934, as amended, filed on April 29, 2013;
- the description of our common stock contained in our Registration Statement on Form 8-A filed on January 26, 2007, including any amendment or report filed for the purpose of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Securities Exchange Act of 1934, as amended, after the date of this prospectus supplement and prior to the termination of this offering shall be deemed to be incorporated by reference in this prospectus supplement and to be a part hereof from the date of filing such reports and other documents.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Investor Relations, Synta Pharmaceuticals Corp., 45 Hartwell Avenue, Lexington, MA 02421, (781) 274-8200.

PROSPECTUS

SYNTA PHARMACEUTICALS CORP.

**\$300,000,000
COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
RIGHTS
PURCHASE CONTRACTS
UNITS**

This prospectus will allow us to issue, from time to time at prices and on terms to be determined at or prior to the time of the offering, up to \$300,000,000 of any combination of the securities described in this prospectus, either individually or in units. We may also offer common stock or preferred stock upon conversion of or exchange for the debt securities; common stock upon conversion of or exchange for the preferred stock; common stock, preferred stock or debt securities upon the exercise of warrants, rights or performance of purchase contracts; or any combination of these securities upon the performance of purchase contracts.

This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide you with the specific terms of any offering in one or more supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any prospectus supplement, as well as any documents incorporated by reference into this prospectus or any prospectus supplement, carefully before you invest.

Our securities may be sold directly by us to you, through agents designated from time to time or to or through underwriters or dealers. 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 or agents are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common stock is listed on The NASDAQ Global Market under the symbol "SNTA." On May 1, 2013, the last reported sale price of our common stock was \$10.25 per share. 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 securities exchange of the securities covered by the prospectus supplement. Prospective purchasers of our securities are urged to obtain current information as to the market prices of our securities, where applicable.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 4 of this prospectus under the caption "Risk Factors." We may include specific risk factors in supplements to this prospectus under the caption "Risk Factors." This prospectus may not be used to sell our securities unless accompanied by 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 May 1, 2013.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants, rights or purchase contracts to purchase any of such securities, either individually or in units, in one or more offerings, with a total value of up to \$300,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of the securities, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained or incorporated by reference in this prospectus. However, no prospectus supplement will offer a security that is not registered and described in this prospectus at the time of its effectiveness. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to the offering of securities under this prospectus. You should carefully read this prospectus, the applicable prospectus supplement, the information and documents incorporated herein by reference and the additional information under the heading "Where You Can Find More Information" before making an investment decision.

You should rely only on the information we have provided or incorporated by reference in this prospectus or any prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained or incorporated by reference in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated herein by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus or any sale of a security.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

This prospectus may not be used to consummate sales of our securities, unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies between any prospectus supplement, this prospectus and any documents incorporated by reference, the document with the most recent date will control.

Unless the context otherwise requires, "Synta," "the Company," "we," "us," "our" and similar terms refer to Synta Pharmaceuticals Corp. and our subsidiaries.

Our trademarks include, without limitation, Synta Pharmaceuticals, our corporate logo and the GALAXY Trial. Other service marks, trademarks and trade names contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and therein are the property of their respective owners.

PROSPECTUS SUMMARY

The following is a summary of what we believe to be the most important aspects of our business and the offering of our securities under this prospectus. We urge you to read this entire prospectus, including the more detailed consolidated financial statements, notes to the consolidated financial statements and other information incorporated by reference from our other filings with the SEC or included in any applicable prospectus supplement. Investing in our securities involves risks. Therefore, carefully consider the risk factors set forth in any prospectus supplements and in our most recent annual and quarterly filings with the SEC, as well as other information in this prospectus and any prospectus supplements and the documents incorporated by reference herein or therein, before purchasing our securities. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities.

About Synta Pharmaceuticals Corp.

We are a biopharmaceutical company focused on discovering, developing, and commercializing small molecule drugs to extend and enhance the lives of patients with severe medical conditions, including cancer and chronic inflammatory diseases. We have two drug candidates in clinical trials for treating multiple types of cancer and several drug candidates in the preclinical stage of development. Each of our drug candidates was discovered and developed internally using our proprietary, unique chemical compound library and integrated discovery engine. We retain full ownership of all of our drug candidates.

We believe that the broad clinical and commercial potential of our drug candidates, together with our operational capabilities and additional competitive advantages, provide us with multiple, sustainable growth opportunities. Our capabilities and advantages include: our intellectual property portfolio, consisting of over 700 issued and pending patents; the full ownership of all commercial rights in all geographic regions to our programs; our ability to integrate discovery, translational, and clinical research to optimize our development programs and further strengthen our intellectual property position; our operational experience in effectively managing large-scale, global clinical programs; our strong network of relationships with leading investigators and medical centers; our proprietary chemical compound library and the strength of our drug discovery platform; and the skills, talent, and level of industry experience of our employees.

Additional Information

We commenced operations in July 2001. In September 2002, we acquired Principia Associates, Inc., which had previously acquired Shionogi BioResearch Corp., a U.S.-based drug discovery subsidiary of the Japanese pharmaceutical company, Shionogi & Co., Ltd. In this acquisition, we acquired a unique chemical compound library, an integrated set of drug discovery capabilities, and a pipeline of preclinical and research programs. Since 2002, we have been advancing these programs into later stages of development, discovering and developing additional drug candidates and expanding our management and scientific teams and capabilities to support more advanced stages of drug development and commercialization.

Our principal executive offices are located at 45 Hartwell Avenue, Lexington, Massachusetts 02421, and our telephone number is (781) 274-8200. Our website address is www.syntapharma.com. The information contained on our website is not incorporated by reference into, and does not form any part of, this prospectus supplement or the accompanying prospectus. We have included our website address as a factual reference and do not intend it to be an active link to our website. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available free of charge through the "Investors—SEC Filings" section of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC.

Offerings Under This Prospectus

Under this prospectus, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants, rights or purchase contracts to purchase any of such securities, either individually or in units, with a total value of up to \$300,000,000, from time to time at prices and on terms to be determined by market conditions at the time of the offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
- aggregate principal amount or aggregate offering price;
- maturity, if applicable;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion or sinking fund terms, if any;
- voting or other rights, if any; and
- conversion or exercise prices, if any.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. However, no prospectus supplement will offer a security that is not registered and described in this prospectus at the time of its effectiveness.

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

- the names of those agents or underwriters;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us.

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

RISK FACTORS

Investing in our securities involves significant risk. The prospectus supplement applicable to each offering of our securities may contain a discussion of the risks applicable to an investment in Synta. Prior to making a decision about investing in our securities, you should carefully consider the specific factors discussed under the heading "Risk Factors" in the applicable prospectus supplement, together with all of the other information contained or incorporated by reference in the prospectus supplement or appearing or incorporated by reference in this prospectus. You should also consider the risks, uncertainties and assumptions discussed under the heading "Risk Factors" included in our most recent annual report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K on file with the SEC, all of which are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

RATIO OF EARNINGS TO FIXED CHARGES

Any time debt securities are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

The SEC encourages companies to disclose forward-looking information so that investors can better understand a company's future prospects and make informed investment decisions. This prospectus and the documents we have filed with the SEC that are incorporated herein by reference contain such "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995.

Such statements in connection with any discussion of future operations or financial performance are identified by the use of words such as "may," "anticipate," "estimate," "expect," "project," "intend," "plan," "believe," and other words and terms of similar meaning. Such statements are based on management's expectations and are subject to certain factors, risks and uncertainties that may cause actual results, outcome of events, timing and performance to differ materially from those expressed or implied by such statements. These risks and uncertainties include, but are not limited to, the risk that we may be unable to develop and achieve commercial success for our drug candidates; the risk that we may be unable to discover drugs that are safer and more efficacious than our competitors; the risk that we may be unable to establish and maintain manufacturing capabilities for our products; the possibility of delays in the research and development necessary to select drug development candidates and delays in clinical trials; the risk that clinical trials may not result in marketable products; the risk that we may be unable to successfully finance and secure regulatory approval of and market our drug candidates, or that clinical trials will not be completed on the timelines we have estimated; uncertainties about our ability to obtain new corporate collaborations and acquire new technologies on satisfactory terms, if at all; the development of competing products and services; the risk that we may be unable to protect our proprietary technologies; the risk of patent-infringement claims; risks of new, changing and competitive technologies and regulations in the United States and internationally; and other factors detailed under the heading "Risk Factors" in this prospectus as updated and supplemented by the discussion of risks and uncertainties under "Risk Factors" contained in any supplements to this prospectus and in our most recent annual report on Form 10-K, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K, as well as any amendments thereto, as filed with the SEC and which are incorporated herein by reference. The information contained in this document is believed to be current as of the date of this document. We do not intend to update any of

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the forward-looking statements after the date of this document to conform these statements to actual results or to changes in our expectations, except as required by law.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this prospectus or in any document incorporated herein by reference might not occur. Investors are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this prospectus or the date of the document incorporated by reference in this prospectus. We are not under any obligation, and we expressly disclaim any obligation, to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise. All subsequent forward-looking statements attributable to us or to any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

USE OF PROCEEDS

We cannot assure you that we will receive any proceeds in connection with securities which may be offered pursuant to this prospectus. Unless otherwise indicated in the applicable prospectus supplement, we intend to use any net proceeds from the sale of securities under this prospectus for our operations and for other general corporate purposes, including, but not limited to, repayment or refinancing of existing indebtedness or other corporate borrowings, working capital, intellectual property protection and enforcement, capital expenditures, investments, acquisitions or collaborations, repurchases and redemption of our securities, research and development and product development. We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. As a result, our management will have broad discretion to allocate the net proceeds, if any, we receive in connection with securities offered pursuant to this prospectus for any purpose. Pending application of the net proceeds as described above, we may initially invest the net proceeds in short-term, investment-grade, interest-bearing securities or apply them to the reduction of short-term indebtedness.

PLAN OF DISTRIBUTION

We may offer securities under this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities (1) through underwriters or dealers, (2) through agents or (3) directly to one or more purchasers, or through a combination of such methods. We may distribute the securities from time to time in one or more transactions at:

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

We may directly solicit offers to purchase the securities being offered by this prospectus. We may also designate agents to solicit offers to purchase the securities from time to time. We will name in a prospectus supplement any underwriter or agent involved in the offer or sale of the securities.

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

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale, and we will provide the name of any underwriter in the prospectus supplement which the underwriter will use to make resales

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of the securities to the public. In connection with the sale of the securities, we, or the purchasers of the securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

With respect to underwritten public offerings, negotiated transactions and block trades, we will provide in the applicable prospectus supplement information regarding any compensation we pay to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, or the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

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

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

Shares of our common stock sold pursuant to the registration statement of which this prospectus is a part will be authorized for quotation and trading on The NASDAQ Global Market. 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 securities exchange of the securities covered by the prospectus supplement. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

In order to facilitate the offering of the securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing the applicable security in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a

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level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc., 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.

The underwriters, dealers and agents may engage in other transactions with us, or perform other services for us, in the ordinary course of their business.

DESCRIPTION OF COMMON STOCK

We are authorized to issue 100,000,000 shares of common stock, par value \$0.0001 per share. On March 8, 2013, we had 69,054,951 shares of common stock outstanding and approximately 63 stockholders of record.

The following summary of certain provisions of our common stock does not purport to be complete. You should refer to our restated certificate of incorporation and our restated bylaws, both of which are included as exhibits to the registration statement of which this prospectus is a part. The summary below is also qualified by provisions of applicable law.

General

Holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders, and do not have cumulative voting rights. Subject to preferences that may be applicable to any outstanding shares of preferred stock, holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of funds legally available for dividend payments. All shares of common stock outstanding as of the date of this prospectus and, upon issuance and sale, all shares of common stock that we may offer pursuant to this prospectus, will be fully paid and nonassessable. The holders of common stock have no preferences or rights of conversion, exchange, pre-emption or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. In the event of any liquidation, dissolution or winding-up of our affairs, holders of common stock will be entitled to share ratably in our assets that are remaining after payment or provision for payment of all of our debts and obligations and after liquidation payments to holders of outstanding shares of preferred stock, if any.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

NASDAQ Global Market

Our common stock is listed for quotation on The NASDAQ Global Market under the symbol "SNTA."

DESCRIPTION OF PREFERRED STOCK

We are authorized to issue 5,000,000 shares of preferred stock, par value \$0.0001 per share. As of March 8, 2013, no shares of our preferred stock were outstanding or designated. The following summary of certain provisions of our preferred stock does not purport to be complete. You should refer to our restated certificate of incorporation and our restated bylaws, both of which are included as exhibits to the registration statement of which this prospectus is a part. The summary below is also qualified by provisions of applicable law.

General

Our board of directors may, without further action by our stockholders, from time to time, direct the issuance of shares of preferred stock in series and may, at the time of issuance, determine the rights, preferences and limitations of each series, including voting rights, dividend rights and redemption and liquidation preferences. Satisfaction of any dividend preferences of outstanding shares of preferred stock would reduce the amount of funds available for the payment of dividends on shares of our common stock. Holders of shares of preferred stock may be entitled to receive a preference payment in the event of any liquidation, dissolution or winding-up of our company before any payment is made to the holders of shares of our common stock. In some circumstances, the issuance of shares of preferred stock may render more difficult or tend to discourage a merger, tender offer or proxy contest, the assumption of control by a holder of a large block of our securities or the removal of incumbent management. Upon the affirmative vote of our board of directors, without stockholder approval, we may issue shares of preferred stock with voting and conversion rights which could adversely affect the holders of shares of our common stock.

If we offer a specific series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

- the title and stated value;
- the number of shares offered, the liquidation preference, if any, per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption, if applicable;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated) and exchange period;
- voting rights, if any, of the preferred stock;

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- a discussion of any material and/or special U.S. 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 liquidation, dissolution or winding up of the affairs of Synta; and
- any material limitations on issuance of any class or series of preferred stock ranking pari passu with or senior to the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of Synta.

Transfer Agent and Registrar

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

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplements, 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 apply generally to any future debt securities we may offer pursuant to this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any debt securities offered under such prospectus supplement may differ from the terms we describe below, and to the extent the terms set forth in a prospectus supplement differ from the terms described below, the terms set forth in the prospectus supplement shall control.

We may sell from time to time, in one or more offerings under this prospectus, debt securities, which may be senior or subordinated. We will issue any such senior debt securities under a senior indenture that we will enter into with a trustee to be named in the senior indenture. We will issue any such subordinated debt securities under a subordinated indenture, which we will enter into with a trustee to be 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 either the senior indenture or the subordinated indenture, as applicable. The indentures will be qualified under the Trust Indenture Act of 1939, as in effect on the date of the indenture. We use the term "debenture trustee" to refer to either the trustee under the senior indenture or the trustee under the subordinated indenture, as applicable.

The following summaries of material provisions of the senior debt securities, the subordinated debt securities 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.

General

Each indenture provides that debt securities may be issued from time to time in one or more series and may be denominated and payable in foreign currencies or units based on or relating to foreign currencies. Neither indenture limits the amount of debt securities that may be issued thereunder, and each indenture provides that the specific terms of any series of debt securities shall be set forth in, or determined pursuant to, an authorizing resolution and/or a supplemental indenture, if any, relating to such series.

We will describe in each prospectus supplement the following terms relating to a series of debt securities:

- the title or designation;

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- the aggregate principal amount and any limit on the amount that may be issued;
- the currency or units based on or relating to currencies in which debt securities of such series are denominated and the currency or units in which principal or interest or both will or may be payable;
- whether we will issue the series of debt securities in global form, the terms of any global securities and who the depositary will be;
- the maturity date and the date or dates on which principal will be payable;
- the interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the date or dates interest will be payable and the 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;
- the place or places where payments will be payable;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking 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 to pay dividends, or will require us to maintain any asset ratios or reserves;
- whether we will be restricted from incurring any additional indebtedness;
- a discussion on any material or special U.S. federal income tax considerations applicable to a series of debt securities;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

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

Conversion or Exchange Rights

We will set forth in the prospectus supplement the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common

stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger or Sale; No Protection in Event of a Change of Control or Highly Leveraged Transaction

The indentures do not contain any covenant that 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 to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate.

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

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 our failure continues for 90 days and the time for payment has not been extended or deferred;
- if we fail to pay the principal, or premium, if any, when due and the time for payment has not been extended or delayed;
- if we fail to observe or perform any other covenant set forth in the debt securities of such series or the applicable indentures, other than a covenant specifically relating to and for the benefit of holders of another series of debt securities, and our failure continues for 90 days after we receive written notice from the debenture trustee or holders of not less than a majority in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur as to us.

No event of default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an event of default with respect to any other series of debt securities. The occurrence of an event of default may constitute an event of default under any bank credit agreements we may have in existence from time to time. In addition, the occurrence of certain events of default or an acceleration under the indenture may constitute an event of default under certain of our other indebtedness outstanding from time to time.

If an event of default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than a majority in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the debenture trustee if given by the holders), declare to be due and payable immediately the principal (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) of and premium and accrued and unpaid interest, if any, on all debt securities of that series. Before a judgment or decree for payment of the money due has been obtained with respect to debt securities of any series, the holders of a majority in principal amount of the outstanding debt securities of that series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may rescind and annul the acceleration if all events of default, other than the non-payment of accelerated principal, premium, if any, and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the applicable indenture (including

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payments or deposits in respect of principal, premium or interest that had become due other than as a result of such acceleration). We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an event of default.

Subject to the terms of the indentures, if an event of default under an indenture shall occur and be continuing, the debenture trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the 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, 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 previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;
- the holders of at least a majority 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 (or at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) other conflicting directions within 60 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 applicable debenture trustee regarding our compliance with specified covenants in the applicable indenture.

Modification of Indenture; Waiver

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

- to fix any ambiguity, defect or inconsistency in the indenture; and
- to change anything that does not materially adversely affect the interests of any holder of debt securities of any series issued pursuant to such indenture.

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 (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of

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the debt securities of such series represented at such meeting) that is affected. However, the debenture trustee and we may make the following changes only 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 any premium payable upon the redemption of any debt securities;
- reducing the principal amount of discount securities payable upon acceleration of maturity;
- making the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver.

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series (or, at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. The holders of a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series or in respect of a covenant or provision, which cannot be modified or amended without the consent of the holder of each outstanding debt security of the series affected; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration.

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 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;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

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

Form, Exchange, and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, 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

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behalf of, The Depository Trust Company or another depository named by us and identified in a prospectus supplement with respect to that series.

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, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indentures and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange or in the applicable indenture, 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 the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

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

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning the Debenture Trustee

The debenture trustee, other than during the occurrence and continuance of an event of default under the applicable 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 under such indenture 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 the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

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

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

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office 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 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 security thereafter may look only to us for payment thereof.

Governing Law

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

Subordination of Subordinated Debt Securities

Our obligations pursuant to any subordinated debt securities will be unsecured and will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. The subordinated indenture does not limit the amount of senior indebtedness we may incur. It also does not limit us from issuing any other secured or unsecured debt.

DESCRIPTION OF WARRANTS

General

We may issue warrants to purchase shares of our common stock, preferred stock and/or debt securities in one or more series together with other securities or separately, as described in the applicable prospectus supplement. Below is a description of certain general terms and provisions of the warrants that we may offer. Particular terms of the warrants will be described in the warrant agreements and the prospectus supplement relating to the warrants.

The applicable prospectus supplement will contain, where applicable, the following terms of and other information relating to the warrants:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that series of our preferred stock;
- if applicable, the exercise price for our debt securities, the amount of debt securities to be received upon exercise, and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;

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- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants may be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Transfer Agent and Registrar

The transfer agent and registrar for any warrants will be set forth in the applicable prospectus supplement.

DESCRIPTION OF RIGHTS

General

We may issue rights to our stockholders to purchase shares of our common stock, preferred stock or the other securities described in this prospectus. We may offer rights separately or together with one or more additional rights, debt securities, preferred stock, common stock, warrants or purchase contracts, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the rights to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the rights, rights agreement or rights certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable rights agreement and rights certificate for additional information before you decide whether to purchase any of our rights.

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We will provide in a prospectus supplement the following terms of the rights being issued:

- the date of determining the stockholders entitled to the rights distribution;
- the aggregate number of shares of common stock, preferred stock or other securities purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- whether the rights are transferrable and the date, if any, on and after which the rights may be separately transferred;
- the date on which the right to exercise the rights will commence, and the date on which the right to exercise the rights will expire;
- the method by which holders of rights will be entitled to exercise;
- the conditions to the completion of the offering, if any;
- the withdrawal, termination and cancellation rights, if any;
- whether there are any backstop or standby purchaser or purchasers and the terms of their commitment, if any;
- whether stockholders are entitled to oversubscription rights, if any;
- any applicable U.S. federal income tax considerations; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights, as applicable.

Each right will entitle the holder of rights to purchase for cash the principal amount of shares of common stock, preferred stock or other securities at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock, preferred stock or other securities, as applicable, purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Rights Agent

The rights agent for any rights we offer will be set forth in the applicable prospectus supplement.

DESCRIPTION OF PURCHASE CONTRACTS

We may issue purchase contracts, including contracts obligating holders to purchase from us, and for us to sell to holders, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants or rights, or securities of an entity unaffiliated with us, or any combination of the above, at a future date or dates. Alternatively, the purchase contracts may obligate us to purchase from holders, and obligate holders to sell to us, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants, rights or other property, or any combination of the

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above. The price of the securities or other property subject to the purchase contracts may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula described in the purchase contracts. We may issue purchase contracts separately or as a part of units each consisting of a purchase contract and one or more of our other securities described in this prospectus or securities of third parties, including U.S. Treasury securities, securing the holder's obligations under the purchase contract. The purchase contracts may require us to make periodic payments to holders or vice versa and the payments may be unsecured or pre-funded on some basis. The purchase contracts may require holders to secure the holder's obligations in a manner specified in the applicable prospectus supplement.

The applicable prospectus supplement will describe the terms of any purchase contracts in respect of which this prospectus is being delivered, including, to the extent applicable, the following:

- whether the purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;
- whether the purchase contracts are to be prepaid;
- whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance or level of the securities subject to purchase under the purchase contract;
- any acceleration, cancellation, termination or other provisions relating to the settlement of the purchase contracts;
- any applicable U.S. federal income tax considerations; and
- whether the purchase contracts will be issued in fully registered or global form.

The preceding description sets forth certain general terms and provisions of the purchase contracts to which any prospectus supplement may relate. The particular terms of the purchase contracts to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the purchase contracts so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the purchase contracts described in a prospectus supplement differ from any of the terms described above, then the terms described above will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable purchase contract for additional information before you decide whether to purchase any of our purchase contracts.

DESCRIPTION OF UNITS

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

We will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units consisting of common stock, preferred stock, one or more debt securities, warrants, rights or purchase contracts for the purchase of common stock, preferred stock and/or debt securities in one or more series, in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each security included in the unit. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

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

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those set forth in any prospectus supplement or as described under "Description of Common Stock," "Description of Preferred Stock," "Description of Debt Securities," "Description of Warrants," "Description of Rights" and "Description of Purchase Contracts" will apply to each unit, as applicable, and to any common stock, preferred stock, debt security, warrant, right or purchase contract included in each unit, as applicable.

Unit Agent

The name and address of the unit agent for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in such numerous distinct series as we determine.

Enforceability of Rights by Holders of Units

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

CERTAIN PROVISIONS OF DELAWARE LAW AND OF THE COMPANY'S CERTIFICATE OF INCORPORATION AND BYLAWS

Anti-Takeover Provisions of our Certificate of Incorporation and Bylaws

In addition to the board of directors' ability to issue shares of preferred stock, our restated certificate of incorporation and restated bylaws contain other provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of our company unless such takeover or change in control is approved by our board of directors.

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These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Classified board of directors; removal of directors for cause. Our restated certificate of incorporation and restated bylaws provide for our board of directors to be divided into three classes serving staggered terms. At each annual meeting of stockholders, directors elected to succeed those directors whose terms expire will be elected for a three-year term of office. All directors elected to our classified board of directors will serve until the election and qualification of their respective successors or their earlier resignation or removal. The board of directors is authorized to create new directorships and to fill such positions so created and is permitted to specify the class to which any such new position is assigned. The person filling such position would serve for the term applicable to that class. The board of directors (or its remaining members, even if less than a quorum) is also empowered to fill vacancies on the board of directors occurring for any reason for the remainder of the term of the class of directors in which the vacancy occurred. Members of the board of directors may only be removed for cause and only by the affirmative vote of 80% of our outstanding voting stock. These provisions are likely to increase the time required for stockholders to change the composition of the board of directors. For example, in general, at least two annual meetings will be necessary for stockholders to effect a change in a majority of the members of the board of directors. The provision for a classified board could prevent a party who acquires control of a majority of our outstanding common stock from obtaining control of our board of directors until our second annual stockholders meeting following the date the acquirer obtains the controlling stock interest. The classified board provision could have the effect of discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us and could increase the likelihood that incumbent directors will retain their positions.

Advance notice provisions for stockholder proposals. Our restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors, as well as procedures for including proposed nominations at special meetings at which directors are to be elected. Stockholders at our annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given to our secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting, and who has complied with the procedures and requirements set forth in the bylaws. Although our bylaws do not give our board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, our bylaws may have the effect of precluding the conduct of some business at a meeting if the proper procedures are not followed or may discourage or defer a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of us.

Special meetings of stockholders. Special meetings of the stockholders may be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors. Stockholders are not permitted to call a special meeting or to require our board of directors to call a special meeting.

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No stockholder action by written consent. Our restated certificate of incorporation and restated bylaws do not permit our stockholders to act by written consent. As a result, any action to be effected by our stockholders must be effected at a duly called annual or special meeting of the stockholders.

Super-majority stockholder vote required for certain actions. The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless the corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our restated certificate of incorporation requires the affirmative vote of the holders of at least 80% of our outstanding voting stock to amend or repeal certain provisions of our restated certificate of incorporation. This 80% stockholder vote would be in addition to any separate class vote that might in the future be required pursuant to the terms of any preferred stock that might then be outstanding. In addition, an 80% vote is also required for any amendment to, or repeal of, our restated bylaws by the stockholders. Our restated bylaws may be amended or repealed by a vote of a majority of the total number of authorized directors.

Provisions of Delaware Law Governing Business Combinations

We are subject to the "business combination" provisions of Section 203 of the Delaware General Corporation Law. In general, such provisions prohibit a publicly held Delaware corporation from engaging in any "business combination" transactions with any "interested stockholder" for a period of three years after the date on which the person became an "interested stockholder," unless:

- prior to such date, the board of directors approved either the "business combination" or the transaction which resulted in the "interested stockholder" obtaining such status; or
- upon consummation of 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 voting stock outstanding (but not the outstanding voting stock owned by the "interested stockholder") those shares owned by (a) persons who are directors and also officers and (b) employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- at or subsequent to such time the "business combination" is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least $66\frac{2}{3}\%$ of the outstanding voting stock which is not owned by the "interested stockholder."

A "business combination" is defined to include mergers, asset sales and other transactions resulting in financial benefit to a stockholder. In general, an "interested stockholder" is a person who, together with affiliates and associates, owns 15% or more of a corporation's voting stock or within three years did own 15% or more of a corporation's voting stock. The statute could prohibit or delay mergers or other takeover or change in control attempts with respect to us and, accordingly, may discourage attempts to acquire us.

Limitations on Liability and Indemnification of Officers and Directors

Our restated certificate of incorporation limits the liability of our officers and directors to the fullest extent permitted by the Delaware General Corporation Law, and our restated certificate of incorporation and restated bylaws provide that we will indemnify our officers and directors to the fullest extent permitted by such law. We have also entered into indemnification agreements with our officers and directors and expect to enter into a similar agreement with any new officers and directors.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, will pass upon the validity of the issuance of the securities offered by this prospectus.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2012, and the effectiveness of our internal control over financial reporting as of December 31, 2012, 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 are subject to the reporting 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 may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's web site at <http://www.sec.gov>. Our common stock is listed on The NASDAQ Global Market, and you can read and inspect our filings at the offices of the Financial Industry Regulatory Authority at 1735 K Street, Washington, D.C. 20006.

This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act of 1933, as amended, and therefore omits certain information contained in the registration statement. We have also filed exhibits and schedules with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit or schedule for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits and schedules, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

We also maintain a website at www.syntapharma.com, through which you can access our SEC filings. The information set forth on our website is not part of this prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form S-3 under the Securities Act of 1933, as amended, with the SEC with respect to the securities we may offer pursuant to this prospectus. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the

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exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where You Can Find More Information." The documents we are incorporating by reference are:

- our Annual Report on Form 10-K for the year ended December 31, 2012, filed on March 14, 2013;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2013 filed on April 30, 2013;
- our Current Reports on Form 8-K, filed on March 8, 2013, March 13, 2013 and April 1, 2013;
- the portions of our Definitive Proxy Statement on Schedule 14A filed on April 29, 2013 that are deemed "filed" with the SEC under the Exchange Act;
- the description of our common stock contained in our Registration Statement on Form 8-A filed on January 26, 2007, including any amendment or report filed for the purpose of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

The SEC file number for each of the documents listed above is 001-33277.

Any statement contained in this prospectus or in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

You may request, orally or in writing, a copy of any or all of the documents incorporated herein by reference. These documents will be provided to you at no cost, by contacting: Investor Relations, Synta Pharmaceuticals Corp., 45 Hartwell Avenue, Lexington, MA 02421, (781) 274-8200.

You should rely only on information contained in, or incorporated by reference into, this prospectus and any prospectus supplement. We have not authorized anyone to provide you with information different from that contained in this prospectus or incorporated by reference in this prospectus. We are not making offers to sell the securities in any jurisdiction in which such an offer or solicitation is not authorized or in which the person making such offer or solicitation is not qualified to do so or to anyone to whom it is unlawful to make such offer or solicitation.

Shares



Common Stock

PROSPECTUS SUPPLEMENT

Sole Book-Running Manager

Jefferies

November , 2013
