Filed Pursuant to Rule 424(b)(5)
Registration No. 333-152833

PROSPECTUS SUPPLEMENT

(To Prospectus dated August 28, 2008)

5,555,556 Shares of Common Stock

We are offering 5,555,556 shares of our common stock in this offering.

Our common stock is listed on The NASDAQ Global Market under the symbol "SNTA." On January 7, 2010, the last reported sale price of our common stock was $5.46 per share.

Investing in our common stock involves significant risks. See "Risk Factors" beginning on page S-9 of this prospectus supplement and page 6 of the accompanying prospectus.

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

	Per Share	Total
Public offering price	$4.50	$25,000,002
Underwriting discounts and commissions	$0.27	$ 1,500,000
Proceeds to Synta (before expenses)	$4.23	$23,500,002

We estimate the total expenses of this offering, excluding the underwriting discounts and commissions, will be approximately $400,000. We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to a total of 833,333 additional shares of our common stock at the public offering price per share, less the underwriting discounts and commissions, to cover any over-allotments.

We anticipate that delivery of the shares will be made on or about January 13, 2010, subject to customary closing conditions.

Sole Book-Running Manager

LAZARD CAPITAL MARKETS

Co-Manager

RBC CAPITAL MARKETS

Prospectus Supplement dated January 8, 2010.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is the prospectus supplement, which describes the specific terms of the securities we are offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. This prospectus supplement and the accompanying prospectus and the documents incorporated by reference herein and therein are part of a shelf registration statement that we filed with the Securities and Exchange Commission. Under the shelf registration process, we may offer from time to time shares of our common stock and other securities up to an aggregate amount of $150,000,000, of which this offering is a part. This prospectus supplement and the accompanying prospectus and the documents incorporated by reference herein and therein include important information about us, our securities being offered and other information you should know before investing. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any related free writing prospectus that we authorized to be delivered to you, as well as the additional information described under "Where You Can Find More Information" on page S-16 of this prospectus supplement and "Incorporation of Documents by Reference" on page S-16 of this prospectus supplement before investing in our securities.

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

You should rely only on the information contained in this prospectus supplement, the accompanying prospectus, any related free writing prospectus that we authorized to be distributed to you and the documents incorporated by reference herein and therein. We have not, and the underwriters have not, authorized anyone to provide you with information that is different. If anyone provides you with different or inconsistent information, you should not rely on it. We are offering to sell and seeking offers to buy shares of our common stock only in jurisdictions where offers and sales are permitted. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information contained in this prospectus supplement, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus and any related free writing prospectus that we have authorized to be delivered to you is accurate only as of their respective dates, regardless of the time of delivery of such documents or of any sale of securities. Our business, financial condition, results of operations and prospects may have changed since those dates. You should not consider this prospectus supplement or the accompanying prospectus to be an offer or solicitation relating to the securities in any jurisdiction in which such an offer or solicitation relating to the securities is not authorized. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus outside the United States. Furthermore, you should not consider this prospectus supplement or the accompanying prospectus to be an offer or solicitation relating to the securities if the person making the offer or solicitation is not qualified to do so, or if it is unlawful for you to receive such an offer or solicitation.

Unless the context requires otherwise, in this prospectus supplement and the accompanying prospectus the terms "Synta," "the Company," "we," "us," "our" and similar names refer to Synta Pharmaceuticals Corp. and its subsidiaries.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and information appearing elsewhere in this prospectus supplement and in the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information that you should consider before investing in shares of our common stock. The following summary is qualified in its entirety by, and should be read in conjunction with, the more detailed information and financial statements and notes thereto appearing elsewhere in this prospectus supplement and the accompanying prospectus. Before you decide to invest in shares of our common stock, to fully understand this offering and its consequences to you, you should carefully read the entire prospectus supplement and the accompanying prospectus carefully, including the risk factors beginning on page S-9 of this prospectus supplement and beginning on page 6 of the accompanying prospectus, and the consolidated financial statements and related notes included in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein.

Synta Pharmaceuticals Corp.

Overview

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 three clinical-stage drug candidates and several drug candidates in the preclinical and discovery stages, each of which has a distinct chemical structure, mechanism of action, and market opportunity. Each of our drug candidates was discovered and developed internally using our proprietary, unique chemical compound library and integrated discovery engine.

We believe that our chemical compound library and research capabilities, our demonstrated ability to generate new drug candidates, our ability to effectively enroll and conduct large-scale clinical trials, and our ability to enter into partnerships with leading multinational pharmaceutical companies are important competitive advantages. We believe that our pipeline of novel drug candidates, together with these competitive advantages, provide us with both near-term and long-term sustainable growth opportunities.

Oncology Programs

We have two clinical-stage programs (one of which is currently on clinical hold) and one preclinical-stage program in oncology.

STA-9090

STA-9090 is a novel, small molecule Hsp90 inhibitor drug candidate that we are developing for the treatment of a variety of both solid tumors and hematological tumors. Inhibition of Hsp90 is an area of great interest in the oncology community because of the broad role played by Hsp90 in maintaining the function of many cancer-promoting proteins. STA-9090 has a unique chemical structure that is distinct from the first generation Hsp90 inhibitors, such as 17-AAG and other ansamycin derivatives. In laboratory studies, STA-9090 has shown potency up to 100 times greater than 17-AAG and an ability to inhibit a broader range of known cancer-promoting kinases. In animal models, STA-9090 has also shown greater potency than 17-AAG, as well as activity in models that are resistant to treatment with first generation Hsp90 inhibitors. In preclinical studies, STA-9090 has been shown to inhibit multiple cancer-promoting kinases with comparable potency to, and a broader activity profile than, widely-used kinase inhibitors such as imatinib (Gleevec), erlotinib (Tarceva), and sunitinib (Sutent). In addition, STA-9090 has shown activity in both *in vitro* and *in vivo* models of cancer that are resistant to these

kinase inhibitors. This activity profile suggests the potential for use in patients who have been previously treated with kinase inhibitors but have relapsed or become resistant to further treatment.

Results presented at the AACR Conference in April 2009 demonstrated the superior potency of STA-9090 when compared to 17-AAG in both *in vitro* and *in vivo* preclinical experiments in lung cancer. The experiments showed that STA-9090 was active in models of lung cancer both sensitive and resistant to treatment with Tarceva; that STA-9090 binds to Hsp90 with higher affinity than 17-AAG; that STA-9090 was more potent and active in a broader range of *in vitro* models of lung cancer than 17-AAG; that STA-9090 down-regulated a number of key client proteins of Hsp90, including AKT, EGFR, ERBB4, IGF-1R, c-MET, PDGFRα, and c-RET, more effectively than 17-AAG; and that STA-9090 is effective in models of lung cancer that are resistant to 17-AAG.

Results presented at the AACR-NCI-EORTC Conference in November 2009 showed that STA-9090 demonstrated strong activity in multiple tumor models, including lung cancer, gastrointestinal stromal tumors (GIST), prostate cancer, colon cancer, breast cancer, gastric cancer, pancreatic cancer, colon cancer, melanoma, acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, B-cell lymphoma, and multiple myeloma. Potent activity was shown in cancers with genetic mutations known to make those cancers highly drug-resistant, such as the BCR-ABL T315I mutation in leukemias, the EGFR T790M mutation in lung cancer, and the KIT Ex 11 V654A and D820A mutations in GIST. STA-9090 was also shown to have potency superior to 17-AAG across multiple tumor models and gene mutation profiles. Results were also presented showing that STA-9090 enhances the activity of the widely used cancer drug paclitaxel.

STA-9090 Ongoing Clinical Trials

We have six ongoing clinical trials for STA-9090:

- *Two Phase 1 trials in solid tumors:* In November 2007 and January 2008, we initiated two Phase 1, open-label studies in patients with solid-tumor cancers to identify the maximum tolerated dose, or MTD, of STA-9090 based on twice- and once-per-week intravenous dosing schedules, respectively. In addition to an evaluation of safety and tolerability, patients in each of these studies are being assessed for evidence of biological activity, as measured by certain biomarkers, and clinical activity, as measured by tumor response.

- *Two Phase 1/2 trials in hematologic cancers:* In March 2009, we initiated a Phase 1/2 open-label clinical study of STA-9090 in patients with hematologic cancers with a twice-per-week dosing schedule. In September 2009, we initiated a Phase 1/2 trial in hematologic cancers with a once-per-week dosing schedule. The Phase 2 portion of the latter trial is focused on evaluating clinical activity in patients with acute myeloid leukemia.

- *Phase 2 trial in non-small cell lung cancer:* In December 2009, we initiated a Phase 2, open-label study in patients with stage IIIB or IV non-small cell lung cancer who have received prior treatment with either an approved tyrosine kinase inhibitor or chemotherapy. Patients in this trial will be stratified into certain cohorts based on the genetic profile of their cancer.

- *Phase 2 trial in gastrointestinal stromal tumors (GIST):* In December 2009, we initiated a Phase 2, open-label study in patients designed to characterize the efficacy and safety of STA-9090 in patients with metastatic or unresectable GIST following failure of systemic treatment with Gleevec and Sutent.

Our choice of dose and schedule for our Phase 2 lung cancer and GIST trials, including the once-per-week administration schedule, has been informed by our results from our Phase 1 trials. The primary objective of these Phase 2 trials is to assess efficacy based on progression-free survival. Additional objectives include assessing tumor response rates, overall survival, the safety and tolerability

of STA-9090 in those patient populations, as well as the impact of treatment with STA-9090 on certain biomarkers.

Our choice of indications for our Phase 2 trials is based on a combination of factors including evidence of clinical activity in our Phase 1 and Phase 1/2 trials; the preclinical data in these cancer indications generated either by ourselves or our academic collaborators; the known scientific rationale for Hsp90 inhibition in these indications; and the level of unmet medical need. We expect to initiate multiple Phase 2 clinical trials for STA-9090 in new indications in the first half of 2010. Many of these trials we expect will be sponsored by investigators, which represent a lower expense to us than company-sponsored trials.

In our Phase 1 solid-tumor trials, the most common adverse events observed have been diarrhea and fatigue, which have been manageable and reversible. These adverse events, diarrhea and fatigue, have been identified as the dose limiting toxicities in our once weekly, solid tumor trial. In the Phase 1 trials we have also seen biomarker activity that has increased with increasing doses of STA-9090. In addition to the acceptable safety profile and encouraging signs of biological activity, we have seen a number of cases of patients who experienced confirmed tumor responses as defined by RECIST criteria, as well as cases of patients who experienced substantial tumor shrinkage and prolonged stabilization of disease, following treatment with STA-9090. These cases of tumor response and stable disease have included patients with lung cancer, renal cancer, melanoma, GIST, colorectal cancer, and a certain type of leukemia. These patients were generally heavily pretreated, and were refractory or resistant to treatment with standard of care drugs. We believe that these preliminary data are encouraging and suggest single agent clinical activity of STA-9090. We expect to present additional results from our ongoing trials at medical meetings in 2010.

Follow on Hsp90 Inhibitors

In 2009, we initiated preclinical development of a follow-on, small molecule, injectable Hsp90 inhibitor. This compound has a unique chemical structure that we believe enhances certain desirable properties. In addition, we are currently working on a new series of Hsp90 inhibitor compounds that may be orally administered. These compounds are in the lead optimization stage.

Elesclomol

Elesclomol is a first-in-class, investigational drug candidate that triggers apoptosis (programmed cell death) in cancer cells. Cancer cells operate at high level of oxidative stress, marked by an elevated presence of reactive oxygen species (ROS) such as oxygen radicals and hydrogen peroxide. Elesclomol is believed to act by increasing the level of oxidative stress in cancer cells even further, beyond sustainable levels, inducing apoptosis. This mechanism of action, called oxidative stress induction, represents a novel way of selectively targeting and killing cancer cells.

In preclinical models, elesclomol showed potent anti-cancer activity against a broad range of cancer cell types, as well as an ability to enhance the efficacy of certain chemotherapy agents with minimal additional toxicity. In September 2006, we reported that in a 21-center, double-blind, randomized, controlled Phase 2b clinical trial in 81 patients with metastatic melanoma, elesclomol in combination with paclitaxel met the primary endpoint—doubling the median time patients survived without their disease progressing—compared to paclitaxel alone ($p=0.035$). Results from this trial were published in the Journal of Clinical Oncology in November 2009.

In November 2007, we announced the initiation of a Phase 3 clinical trial, the SYMMETRY trial, to evaluate treatment with elesclomol plus paclitaxel vs. paclitaxel alone in approximately 630 patients with metastatic melanoma. In February 2009, we suspended our global Phase 3 SYMMETRY trial following a meeting of the independent data monitoring committee, or DMC. The DMC noted that while an interim review of the primary endpoint of progression-free survival, or PFS, showed trends

that favored the elesclomol arm of the study, the interim analysis of the secondary endpoint of overall survival, or OS, favored the control arm. Following our review of the data and further discussion with the DMC, we decided to suspend the SYMMETRY trial and our other ongoing elesclomol trials, including our Phase 1/2 trial in prostate cancer and our Phase 1 single-agent dose-escalating trial for our water-soluble sodium salt formulation, pending further analysis of the SYMMETRY trial results. At that time, at our request, elesclomol was placed on clinical hold by the U.S. Food and Drug Administration, or the FDA, and all trials with elesclomol currently remain on clinical hold.

In our analysis of the SYMMETRY trial results to date, we have not identified any target organ toxicities or adverse events related to elesclomol that might explain an imbalance of deaths between the two arms that was observed at the time of the February DMC meeting. Subsequent analyses showed that in the full patient population treatment with elesclomol did not result in a statistically significant improvement in PFS, the primary endpoint. These analyses did show, however, that in the prospectively-defined subgroup of patients who had normal (≤ 1x Upper Limit of Normal) baseline lactate dehydrogenase (LDH) levels, a recognized prognostic biomarker in melanoma, treatment with elesclomol resulted in a statistically significant improvement in PFS. The normal LDH group constituted 443 patients, or 68% of the total patients enrolled in the trial. These results were presented at the American Society of Clinical Oncology (ASCO) meeting in May 2009. In October 2009, updated elesclomol SYMMETRY trial results, with six months minimum follow up, were presented at the Perspectives in Melanoma XIII Conference. The updated analysis showed that LDH was predictive for treatment with elesclomol for OS as well as PFS: the positive impact of elesclomol treatment on PFS was restricted to patients with normal LDH levels and the negative impact of elesclomol treatment on OS was restricted to patients with high LDH levels. We expect to present SYMMETRY trial data with twelve months minimum follow up later in 2010.

Elesclomol was well-tolerated in the SYMMETRY trial and most observed adverse events were NCI CTC (National Cancer Institute Common Toxicity Criteria) Grade 1 or 2. The most common Grade 3 or higher adverse events in the treatment arm (elesclomol plus paclitaxel) compared to the control arm (paclitaxel alone) were neutropenia (6.8% vs. 2.5%), fatigue (4% vs. 1.2%), anemia (2.2% vs. 1.8%), dyspnea (2.2% vs. 1.8%), alopecia (1.9% vs. 2.8%), peripheral neuropathy (1.9% vs. 1.2%), vomiting (1.9% vs. 1.5%), and infusion related reaction (1.9% vs. 2.2%).

Data presented at the AACR-NCI-EORTC Conference in November 2009 provided new details on the underlying mechanism by which elesclomol elevates oxidative stress. Elesclomol binds copper in plasma, facilitates its uptake into cells, and enables a transition between copper oxidation states once inside the cell. Cancer cells operating at low oxygen, or hypoxic, conditions are known to have different metabolic properties than cancer cells operating under more normal, or normoxic, oxygen conditions. These distinct metabolic properties can impact the oxidation reactions underlying the activity of elesclomol. Because the different metabolic states affect both levels of LDH and elesclomol activity, we are currently investigating whether these differences may have contributed to the results seen in the high vs. low LDH patient populations in our Phase 3 melanoma trial.

In December 2009, we presented the results of a study evaluating the activity of elesclomol against acute myeloid leukemia (AML) cell lines and primary leukemic blast cells from AML patients at the 51st American Society of Hematology (ASH) Annual Meeting and Exposition. The data showed that elesclomol was highly active against AML cell lines and primary blast cells from AML patients at concentrations substantially lower than those already achieved in cancer patients in clinical trials.

Additional survival data, as well as a further understanding of the interaction between oxidative stress induction and LDH levels, will be important for determining the future of the program. In order to continue elesclomol clinical development in the U.S., we would need approval from the FDA to reinitiate clinical trials. While our first pivotal trial for elesclomol was in patients with metastatic melanoma, there were no features unique to melanoma in the collected preclinical and clinical data

that suggested this was the only potential application. Should we restart clinical trials with elesclomol, therefore, metastatic melanoma may not necessarily be the first application. We expect to present more mature SYMMETRY survival data, and announce further decisions related to the future of the elesclomol program in the first half of 2010.

GSK Elesclomol Alliance

In October 2007, as amended in June 2008, we entered into a global collaborative development, commercialization and license agreement with GlaxoSmithKline, or GSK, for the joint development and commercialization of elesclomol under which we received nonrefundable payments, including an $80 million upfront license fee and $50 million in operational milestone payments. On June 10, 2009, following the suspension of the SYMMETRY trial, we received written notice from GSK of their intent to terminate this agreement. The termination of the agreement was effective on September 10, 2009. In accordance with the termination provisions of the agreement, all rights to the elesclomol program have been returned to us as of the effective date of termination. Should we determine to continue the elesclomol program, we may do so either alone or with another partner. Under the termination provisions in the agreement, we may be required to pay GSK a low single-digit royalty on future sales of elesclomol.

STA-9584

STA-9584 is a novel, injectable, small molecule compound that both disrupts the blood vessels that supply tumors with oxygen and essential nutrients, and has direct cytotoxic effects. In preclinical testing, STA-9584 has been shown to target both new and established tumor blood vessels, in contrast to the mechanism of action of angiogenesis inhibitors such as Avastin, which only prevent the formation of new tumor vasculature. STA-9584 has shown strong anti-tumor activity in a broad range of preclinical cancer models, including prostate, lung, breast, melanoma, and lymphoma. This program is currently in preclinical development.

Our Inflammatory Disease Programs

We have one clinical-stage program and one preclinical-stage program 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.

Apilimod (STA-5326)

Apilimod is a novel, orally administered, small molecule drug candidate we are developing for the treatment of autoimmune and other chronic inflammatory diseases. Apilimod inhibits the production of the cytokines interleukin-12, or IL-12, and interleukin-23, or IL-23, and thereby down-regulates the inflammation pathways that underlie certain autoimmune and inflammatory diseases. We submitted the initial investigational new drug application, or IND, for apilimod in March 2003.

We are currently conducting a Phase 2a clinical trial of apilimod in patients with rheumatoid arthritis, or RA. The RA study completed initial enrollment of 22 patients and the preliminary results showed encouraging biomarker and clinical signals suggesting activity of apilimod in this indication. We elected to enroll an additional cohort in this trial to explore a higher dose of apilimod and after enrolling an additional 7 patients into this cohort, we have closed the study to new patients. We expect to have results from this higher dose cohort in the first half of 2010. We are also considering further exploring the possibility of using apilimod in a topical formulation to treat inflammatory diseases of the skin, such as psoriasis.

In addition to apilimod, we have also identified several other small molecule IL-12/23 inhibitors that we believe have comparable activity to apilimod with significantly improved pharmaceutical

properties. We believe that these new compounds represent a promising opportunity to develop next-generation drug candidates that could be administered orally at higher doses than apilimod and potentially address a wider range of serious inflammatory diseases with high unmet medical needs.

CRACM Ion Channel Inhibitors

We have developed novel, small molecule inhibitors of calcium release activated calcium modulator, or CRACM, ion channels expressed on immune cells. The CRACM ion channel is the primary route for calcium entry into T cells and other immune cells, regulating multiple immune cell processes important for initiating and maintaining an inflammatory immune response. Our CRACM ion channel inhibitors have shown strong 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, asthma, chronic obstructive pulmonary disease, or COPD, allergy, transplant rejection, and other autoimmune diseases and inflammatory conditions. This program is in the lead optimization stage. In December 2008, we entered into a global partnership with Hoffman-La Roche, or Roche, to further develop our CRACM inhibitors. We anticipate filing an IND and initiating clinical trials with a CRACM inhibitor in late 2010 or early 2011.

Roche CRACM Inhibitor Alliance

In December 2008, we entered into a collaborative license agreement with Roche to discover, develop, and commercialize small-molecule drugs targeting CRACM channels. The goal is to develop a novel category of oral, disease-modifying agents for the treatment of rheumatoid arthritis, asthma, COPD, allergy, transplant rejection, and other autoimmune diseases and inflammatory conditions. Under the terms of the agreement, Roche will fund research to be conducted by us during an initial two-year research period, which may be extended for additional one year terms by mutual agreement of the parties. Roche will receive worldwide rights to develop and commercialize certain products identified prior to the end of this research period. We retain certain co-development and co-promotion rights. All preclinical, clinical, and commercial costs will be paid by Roche.

Pursuant to the agreement, we received a nonrefundable upfront license payment of $16 million in January 2009, which was recorded as a collaboration receivable as of December 31, 2008. Roche will pay all of our research costs, with a minimum of $9 million in committed research support, and all of our development costs for compounds nominated for clinical development. As of September 30, 2009, we had received approximately $8.7 million in research and development support under this agreement. We are eligible to receive additional payments, for each of three licensed products, should specified development and commercialization milestones be successfully achieved. Development milestones across multiple indications of up to $245 million could be earned for the first product, and up to half of this amount could be earned for each of the second and third products. Commercialization milestones of up to $170 million could be earned for each of three products. In addition, all commercial costs will be paid by Roche. We will receive tiered royalties on sales of all approved, marketed products. Roche may terminate the agreement on a licensed compound-by-licensed compound basis upon providing advance written notice, but may not do so with respect to all licensed compounds until after a specified date.

Company Strategy

Our strategy is to use our proprietary chemical compound library and discovery capabilities, as well as our strength in designing and effectively conducting robust clinical trials, to discover, develop, and

commercialize novel small-molecule drug candidates for treating cancer, autoimmune, and chronic inflammatory diseases. Important elements of our long-term strategy include:

- reducing risk and increasing the probability of clinical and commercial success by maintaining, and continuously replenishing, a drug candidate pipeline that is diversified across distinct mechanism categories, chemical compound families, and therapeutic opportunities;
- using our discovery capabilities to expand and protect our intellectual property position and enhance our competitive advantages for each of these programs, including developing intellectual property associated with related chemical structures, mechanism of action, and method of use;
- using our translational research and biomarker identification capabilities to assist in identifying the most promising patient populations and optimizing the design of clinical trials for our drug candidates;
- maintaining the flexibility to partner or keep individual programs, in order to achieve the balance of fully-owned versus partnered programs that can best enhance long-term shareholder value; and
- maintaining a strong cash position, such that we have the resources and skills to continue both to advance our current pipeline of compounds and replenish our pipeline with new compounds from our discovery engine.

Company History and Corporate 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. We have included our website address as a factual reference and do not intend it to be an active link to our website. Our trademarks include Synta Pharmaceuticals, our corporate logo, SYMMETRY and the SYMMETRY logo. Other service marks, trademarks and trade names appearing in this prospectus supplement and the accompanying prospectus are the property of their respective owners.

The Offering

Common stock offered by us	5,555,556 shares
Over-allotment option	833,333 shares
Common stock to be outstanding after this offering	39,533,856 shares
Use of proceeds	We currently intend to use the net proceeds of this offering for our operations, including, but not limited to, research and development, clinical trials, manufacturing, intellectual property protection and enforcement, and working capital, and for other general corporate purposes, including, but not limited to, repayment of indebtedness, capital expenditures and possible acquisitions. See "Use of Proceeds" on page S-10 of this prospectus supplement.
Risk factors	See "Risk Factors" beginning on page S-9 of this prospectus supplement and on page 6 of the accompanying prospectus for a discussion of factors you should consider carefully when making a decision to invest in our common stock.
NASDAQ Global Market symbol	SNTA

The number of shares of our common stock to be outstanding immediately after this offering as shown above assumes that all of the shares offered hereby are sold and is based on 33,978,300 shares of common stock outstanding as of January 6, 2010. This number of shares does not include 833,333 shares subject to the underwriters' over-allotment option and also excludes the following:

- 4,900,598 shares of our common stock issuable upon exercise of stock options outstanding as of January 6, 2010, at a weighted average exercise price of $8.95; and
- 3,601,133 shares of our common stock available for future awards pursuant to our stock plan as of January 6, 2010.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before purchasing our common stock, you should carefully consider the following risk factors as well as all other information contained in this prospectus supplement and the accompanying prospectus and incorporated by reference, including our consolidated financial statements and the related notes. The risks and uncertainties described below are not the only ones facing us. Additional risks and uncertainties that we are unaware of, or that we currently deem immaterial, also may become important factors that affect us. If any of the following risks occur, our business, financial condition or results of operations could be materially and adversely affected. In that case, the trading price of our common stock could decline, and you may lose some or all of your investment.

Risks Related to this Offering

Management will have broad discretion as to the use of the proceeds from this offering.

We have not designated the amount of net proceeds we will receive from this offering for any particular purpose. Accordingly, our management will have broad discretion as to the application of these net proceeds and could use them for purposes other than those contemplated at the time of this offering. Our stockholders may not agree with the manner in which our management chooses to allocate and spend the net proceeds.

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

You will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering because the price per share of our common stock being offered hereby is substantially higher than the book value per share of our common stock. Based on the public offering price of $4.50 per share in this offering, if you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution of $3.14 per share in the net tangible book value of the common stock. See "Dilution" on page S-11 of this prospectus supplement for a more detailed discussion of the dilution you will incur in this offering.

A substantial number of shares of common stock may be sold in the market following this offering, which may depress the market price for our common stock.

Sales of a substantial number of shares of our common stock in the public market following this offering could cause the market price of our common stock to decline. Immediately following this offering, we will have outstanding an aggregate of 39,533,856 shares of common stock. A substantial majority of the outstanding shares of our common stock are, and all of the shares sold in this offering upon issuance will be, freely tradable without restriction or further registration under the Securities Act of 1933 unless these shares are purchased by affiliates. In addition, as of January 6, 2010, 8,501,731 shares of our common stock are issuable upon exercise of outstanding options or available for issuance under our stock plan.

Additional Risks Related to Our Business, Industry and an Investment in our Common Stock

For a discussion of additional risks associated with our business, our industry and an investment in our common stock, see the section entitled "Risk Factors" of our Annual Report on Form 10-K for the year ended December 31, 2008, which is incorporated by reference into, and deemed to be a part of, this prospectus supplement and the accompanying prospectus.

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 supplement, the accompanying prospectus and the documents incorporated by reference herein and therein contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934.

Words such as "may," "anticipate," "estimate," "expects," "projects," "intends," "plans," "believes" and words and terms of similar substance used in connection with any discussion of future operating or financial performance, identify forward-looking statements. Forward-looking statements represent management's present judgment regarding future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. These risks include, but are not limited to, risks and uncertainties regarding our preclinical studies, our ability to conduct clinical trials of our product candidates and the results of such trials, as well as risks and uncertainties relating to litigation, government regulation and third-party reimbursement, economic conditions, markets, products, competition, intellectual property, services and prices, key employees, future capital needs, dependence on our collaborators and other factors. Please also see the discussion of risks and uncertainties under "Risk Factors" contained in this prospectus supplement and in the accompanying prospectus and in our most recent annual report on Form 10-K, as revised or supplemented by our most recent quarterly report on Form 10-Q, as well as any amendments thereto, as filed with the SEC and which are incorporated herein by reference and our other filings with the SEC incorporated by reference herein.

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 supplement, the accompanying 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 estimate the net proceeds from the sale of common stock by us in this offering will be approximately $23.1 million (or approximately $26.6 million if the underwriters' over-allotment option is exercised in full) after deducting underwriting discounts and commissions and estimated expenses payable by us, based on the public offering price of $4.50 per share.

We currently intend to use the net proceeds from the sale of our common stock for our operations, including, but not limited to, research and development, clinical trials, manufacturing, intellectual property protection and enforcement, and working capital, and for other general corporate purposes, including, but not limited to, repayment of indebtedness, capital expenditures and possible acquisitions. While we have estimated the particular uses for the net proceeds of this offering, 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 for any purpose, and investors will be relying on the judgment of our management with regard to the use of these net proceeds. Pending use of the net proceeds as described above, we intend to invest the net proceeds in short-term, interest-bearing, investment grade securities, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have never paid or declared any cash dividends on our common stock. 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, capital requirements, and other factors that our board of directors deems relevant. In addition, the terms of any future debt or credit facility may preclude us from paying dividends.

DILUTION

The net tangible book value of our common stock on September 30, 2009 was $30.8 million, or $0.91 per share of common stock. Our net tangible book value per share is calculated by subtracting our total liabilities from our total tangible assets and dividing this amount by the number of shares of our common stock outstanding on September 30, 2009.

Based on the sale of the 5,555,556 shares offered hereby at the public offering price of $4.50 per share and after deducting the underwriting discounts and commissions and the estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2009 would have been $53.9 million, or $1.36 per share of our common stock. This represents an immediate increase in net tangible book value of $0.45 per share to our existing stockholders and an immediate dilution in net tangible book value of $3.14 per share to investors participating in this offering. The following table illustrates this per share dilution:

Public offering price per share		$ 4.50
Net tangible book value per share as of September 30, 2009	$ 0.91	
Increase per share attributable to investors participating in this offering	$ 0.45	
As adjusted net tangible book value per share after the offering		1.36
Dilution per share to investors participating in this offering		$ 3.14

The above discussion and table are based on 33,978,300 shares of our common stock outstanding as of September 30, 2009. The information above excludes:

- 4,964,084 shares of our common stock issuable upon exercise of stock options outstanding as of September 30, 2009, at a weighted average exercise price of $8.91; and
- 2,239,121 shares of our common stock available for future awards pursuant to our stock plan as of September 30, 2009.

To the extent options outstanding as of September 30, 2009 have been or may be exercised or other shares have been or are issued, there may be further dilution to new investors.

UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus supplement, the underwriters named below, for whom Lazard Capital Markets LLC is acting as representative, have agreed to purchase, and we have agreed to sell to them, the number of shares of our common stock at the public offering price, less the underwriting discounts and commissions, as set forth on the cover page of this prospectus supplement as indicated below:

Underwriter	Number of Shares
Lazard Capital Markets LLC	4,166,667
RBC Capital Markets Corporation	1,388,889
Total:	5,555,556

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus supplement are subject to the approval of certain legal matters by their counsel and to other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus supplement if any such shares are taken.

The underwriters have an option to buy up to 833,333 additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters may exercise this option at any time and from time to time during the 30-day period from the date of this prospectus supplement. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriters initially propose to offer the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus supplement. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the underwriters. Certain of our directors and entities affiliated with these directors have indicated an interest in purchasing up to an aggregate of 772,222 shares of our common stock in this offering. However, because these indications of interest are not binding agreements or commitments to purchase, these directors and entities may elect not to purchase any shares in this offering.

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of customary legal opinions, letters and certificates.

Commissions and Discounts

The following table summarizes the public offering price, underwriting discounts and commissions and proceeds before expenses to us assuming both no exercise and full exercise of the underwriters' option to purchase additional shares:

		Total	
	Per Share	Without Over-Allotment	With Over-Allotment
Public offering price	$ 4.50	$ 25,000,002	$ 28,750,000
Underwriting discounts and commissions	0.27	1,500,000	1,725,000
Proceeds, before expenses, to us	4.23	23,500,002	27,025,000

The expenses of the offering, not including the underwriting discounts and commissions, payable by us are estimated to be $400,000, which includes $75,000 that we have agreed to reimburse the underwriters for legal fees incurred in connection with this offering. Lazard Frères & Co. LLC referred this transaction to Lazard Capital Markets LLC and will receive a referral fee from Lazard Capital Markets LLC in connection therewith; however, such referral fee is not in addition to the fee paid by us to Lazard Capital Markets LLC described above.

Listing on The NASDAQ Global Market

Our common stock is listed on The NASDAQ Global Market under the symbol "SNTA." Our registrar and transfer agent for all shares of common stock is Computershare Trust Company, N.A.

Indemnification

We and the underwriters have agreed to indemnify each other, and we have also agreed to indemnify Lazard Frères & Co. LLC, against certain liabilities, including liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches of representations and warranties contained in the underwriting agreement. We have also agreed to contribute to payments the underwriters and Lazard Frères & Co. LLC may be required to make in respect of such liabilities.

No Sales of Similar Securities

We, and each of our executive officers and directors, subject to certain exceptions, have agreed with Lazard Capital Markets LLC not to dispose of or hedge any of our shares of common stock or securities convertible into or exercisable or exchangeable for common stock for 90 days after the date of this prospectus supplement without first obtaining the written consent of Lazard Capital Markets LLC. The 90-day "lock-up" period during which we and our executive officers and directors, are restricted from engaging in transactions in our common stock or securities convertible into or exercisable or exchangeable for common stock is subject to extension such that, in the event that either (i) during the last 17 days of the "lock-up" period, we issue an earnings or financial results release or material news or a material event relating to us occurs, or (ii) prior to the expiration of the "lock-up" period, we announce that we will release earnings or financial results during the 16-day period beginning on the last day of the "lock-up" period, then in either case the expiration of the "lock-up" period will be extended until the expiration of the 18-day period beginning on the issuance of the earnings or financial results release or the occurrence of the material news or material event, as applicable, unless Lazard Capital Markets LLC waives, in writing, such an extension.

Price Stabilization, Short Positions

In order to facilitate the offering of our common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. The underwriters must close out any short position by purchasing shares in the open market. A short position may be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchased in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of our common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of our common stock above independent market levels or prevent or slow a decline in the market price of our common stock. The underwriters are not required to engage in these activities, and may end any of these activities at any time.

A prospectus in electronic format may be made available on websites maintained by the underwriters. The underwriters may agree to allocate a number of shares of common stock to other underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters on the same basis as other allocations.

United Kingdom

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order") or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (e) of the Order (all such persons together being referred to as "relevant persons"). The shares of common stock are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such common stock will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 or FSMA) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to us, and

(b) it has complied with, and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

European Economic Area

To the extent that the offer of the common stock is made in any Member State of the European Economic Area that has implemented the Prospectus Directive before the date of publication of a prospectus in relation to the common stock which has been approved by the competent authority in the Member State in accordance with the Prospectus Directive (or, where appropriate, published in accordance with the Prospectus Directive and notified to the competent authority in the Member State in accordance with the Prospectus Directive), the offer (including any offer pursuant to this document) is only addressed to qualified investors in that Member State within the meaning of the Prospectus Directive or has been or will be made otherwise in circumstances that do not require us to publish a prospectus pursuant to the Prospectus Directive.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the "Relevant Implementation Date") it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which 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 competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

(a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities,

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts, or

(c) in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive. For the purposes of this provision, the expression an "offer of shares to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

The EEA selling restriction is in addition to any other selling restrictions set out below. In relation to each Relevant Member State, each purchaser of shares of common stock (other than the underwriters) will be deemed to have represented, acknowledged and agreed that it will not make an offer of shares of common stock to the public in any Relevant Member State, except that it may, with effect from and including the date on which the Prospectus Directive is implemented in the Relevant Member State, make an offer of shares of common stock to the public in that Relevant Member State at any time in any circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive, provided that such purchaser agrees that it has not and will not make an offer of any shares of common stock in reliance or purported reliance on Article 3(2)(b) of the Prospectus Directive. For the purposes of this provision, the expression an "offer of shares to the public" in relation to any shares of common stock in any Relevant Member State has the same meaning as in the preceding paragraph.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, will pass upon the validity of the issuance of the shares of common stock that we are offering. Proskauer Rose LLP, New York, New York is acting as counsel for the underwriters in connection with this offering.

EXPERTS

The consolidated financial statements of Synta Pharmaceuticals Corp. appearing in Synta Pharmaceuticals Corp.'s Annual Report on Form 10-K for the year ended December 31, 2008 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report 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.

The consolidated financial statements of Synta Pharmaceuticals Corp. as of December 31, 2007, and for each of the years in the two-year period ended December 31, 2007, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. KPMG LLP's report includes a paragraph that states that the company adopted Statement of Financial Accounting Standard (SFAS) No. 123R, *Share-Based Payment*, effective January 1, 2006.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, 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. 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 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 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 the accompanying 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 supplement.

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 supplement and the accompanying prospectus, and information that we file later with the SEC will automatically update and supersede this information. Statements in this prospectus supplement and the accompanying 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 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, 2008, filed on March 26, 2009, as amended on November 10, 2009;
- Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2009, filed on May 7, 2009;
- Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2009, filed on August 4, 2009;
- Our Quarterly Report on Form 10-Q for the quarter ended September 30, 2009, filed on November 4, 2009;
- Our Current Report on Form 8-K filed on February 27, 2009;
- Our Current Report on Form 8-K filed on March 18, 2009;
- Our Current Report on Form 8-K filed on April 17, 2009;
- Our Current Report on Form 8-K filed on June 15, 2009;

- Our Current Report on Form 8-K filed on June 19, 2009;
- Our Current Report on Form 8-K filed on July 13, 2009;
- Our Current Report on Form 8-K filed on October 27, 2009;
- Our Current Report on Form 8-K filed on January 8, 2010;
- The portions of our Definitive Proxy Statement on Schedule 14A filed on April 30, 2009 that are deemed "filed" with the SEC under the Exchange Act; and
- 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.

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

In addition, all documents subsequently filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act before the date any offering under this prospectus is terminated or completed are deemed to be incorporated by reference into, and to be a part of, this prospectus.

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.

We will provide, upon written or oral request, without charge to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, a copy of any or all of the information incorporated herein by reference (exclusive of exhibits to such documents unless such exhibits are specifically incorporated by reference herein). Requests, whether written or oral, for such copies should be directed to Secretary: 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.

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PROSPECTUS

SYNTA PHARMACEUTICALS CORP.

$150,000,000
COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
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 $150,000,000 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 the debt securities, common stock upon conversion of the preferred stock, or common stock, preferred stock or debt securities upon the exercise of warrants. We will provide you with specific terms of any offering in one or more supplements to this prospectus. 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 common stock is listed on The Nasdaq Global Market under the symbol "SNTA." On August 28, 2008, the last reported sale price of our common stock was $8.92 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 6 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 offer or sell our securities unless accompanied by a prospectus supplement.

Our securities may be sold directly by us to investors, 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. If any underwriters are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable 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.

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 August 28, 2008.

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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 to purchase any of such securities, either individually or in units, in one or more offerings, with a total value of up to $150,000,000. 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 this offering. You should carefully read this prospectus, the applicable prospectus supplements, 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 names refer to Synta Pharmaceuticals Corp. and our subsidiaries.

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 supplements. Investing in our securities involves risks. Therefore, carefully consider the risk factors 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 a unique chemical compound library, an integrated discovery engine, and a diverse pipeline of clinical- and preclinical-stage drug candidates with distinct mechanisms of action and novel chemical structures. We have three drug candidates in clinical trials, one drug candidate in preclinical studies, and one program in the lead optimization stage of discovery, as well as other programs in earlier stages of discovery. We discovered and developed each of our drug candidates internally using our compound library and discovery capabilities. At present, other than our lead drug candidate, elesclomol, we retain all rights to each of our drug candidates and programs, across all geographic markets and therapeutic indications. We have entered into a partnership with GlaxoSmithKline for the joint development and commercialization of elesclomol.

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 or any accompanying prospectus supplement. We have included our website address as a factual reference and do not intend it to be an active link to our website.

Our trademarks include Synta Pharmaceuticals, our corporate logo, SYMMETRY and the SYMMETRY logo. Other service marks, trademarks and trade names appearing in this prospectus are the property of their respective owners.

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 to purchase any of such securities, either individually or in units, with a total value of up to $150,000,000, from time to time at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities 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;
- conversion prices, if any; and
- important United States federal income tax considerations.

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 fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

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

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.

Common Stock

We may issue shares of our common stock from time to time. The holders of common stock are entitled to one vote per share on all matters to be voted upon by stockholders. Subject to preferences that may be applicable to any outstanding preferred stock, the holders of common stock are entitled to receive ratably any dividends that may be declared from time to time by our board of directors out of funds legally available for that purpose. In the event of our liquidation, dissolution or winding up, the holders of common stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock then outstanding.

Preferred Stock

We may issue shares of our preferred stock from time to time, in one or more series. Our board of directors may determine the rights, preferences, privileges and restrictions of the preferred stock, including dividend rights, conversion rights, preemptive rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock will be convertible into our common stock. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus and applicable prospectus supplements, we will fix the rights, preferences, privileges, qualifications and restrictions of the preferred stock of such series in the certificate of amendment to our certificate of incorporation or the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from a current report on Form 8-K that we file with the SEC, the form of any certificate that describes the terms of the series of preferred stock we are offering before the issuance of the related series of preferred stock. We urge you to read the prospectus supplements related to the series of preferred stock being offered, as well as the complete certificate that contains the terms of the applicable series of preferred stock.

Debt Securities

We may offer debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in priority of payment to certain of our other indebtedness to the extent described in a prospectus supplement. Convertible debt securities will be convertible into or exchangeable for our common stock or our other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the prospectus supplements related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. Forms of indentures have been filed as exhibits to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from a current report on Form 8-K that we file with the SEC, as applicable.

Warrants

We may issue warrants for the purchase of common stock, preferred stock and/or debt securities, in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the prospectus supplements related to the particular series of warrants being offered, as well as the warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants being offered will be filed as exhibits to amendments to the registration statement of which this prospectus is a part, or will be incorporated by reference from a current report on Form 8-K that we file with the SEC, as applicable.

We will evidence each series of warrants by warrant certificates that we will issue under a separate agreement. We will enter into the warrant agreements with a warrant agent. Each warrant agent will be

a bank or trust company that we select. We will indicate the name and address of the warrant agent in the applicable prospectus supplement relating to a particular series of warrants.

Units

We may issue units consisting of common stock, preferred stock, debt securities and/or warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. In this prospectus, we have summarized certain general features of the units. We urge you, however, to read the prospectus supplements related to the series of units being offered, as well as the unit agreements that contain the terms of the units. We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from a current report on Form 8-K that we file with the SEC, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

RISK FACTORS

Investing in our securities involves risk. The prospectus supplement applicable to each offering of our securities will 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, which is on file with the SEC and is 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

We did not record earnings for any of the years ended December 31, 2007, 2006, 2005, 2004 or 2003 or for the six months ended June 30, 2008. Accordingly, our earnings were insufficient to cover fixed charges in such periods and we are unable to disclose a ratio of earnings to fixed charges. The following table sets forth, for each of the periods presented, the dollar amount of the deficiency of earnings available to cover fixed charges. For purposes of computing the deficiency of earnings available to cover fixed charges, fixed charges represent interest expense and an estimate of the interest expense within rental expense.

	Six Months Ended June 30,	Year Ended December 31,				
In thousands	2008	2007	2006	2005	2004	2003
Deficiency of Earnings to Cover Fixed Charges	$ 40,344	$ 63,495	$ 57,270	$ 68,863	$ 45,934	$ 27,878

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.

Words such as "may," "anticipate," "estimate," "expects," "projects," "intends," "plans," "believes" and words and terms of similar substance used in connection with any discussion of future operating or financial performance, identify forward-looking statements. Forward-looking statements represent management's present judgment regarding future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially from those described in the forward-looking statements. These risks include, but are not limited to, risks and uncertainties regarding our preclinical studies, our ability to conduct clinical trials of our product candidates and the results of such trials, as well as risks and uncertainties relating to litigation, government regulation and third-party reimbursement, economic conditions, markets, products, competition, intellectual property, services and prices, key employees, future capital needs, dependence on our collaborators and other factors. Please also see the discussion of risks and uncertainties under "Risk Factors" contained in this prospectus and in any supplements to this prospectus and in our most recent annual report on

Form 10-K, as revised or supplemented by our most recent quarterly report on Form 10-Q, as well as any amendments thereto, as filed with the SEC and which are incorporated herein by reference.

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 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. 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 common stock from time to time in one or more transactions at:

- a fixed price or prices, which may be changed;
- 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 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 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.

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

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 August 1, 2008, we had 33,893,959 shares of common stock outstanding and approximately 106 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 we have filed with the SEC in connection with this offering. 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." On August 28, 2008, the last reported sale price of our common stock was $8.92 per share.

DESCRIPTION OF PREFERRED STOCK

We are authorized to issue 5,000,000 shares of preferred stock, par value $0.0001 per share. As of August 7, 2008, 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 we have filed with the SEC in connection with this offering. 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 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;
- 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 senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of Synta.

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 we offer under that 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, which includes this prospectus. We use the term "indentures" to refer to both the senior indenture and the subordinated indenture. The indentures will be qualified under the Trust Indenture Act of 1939, as in effect on the date of the indenture, or the Trust Indenture Act. We use the term "debenture trustee" to refer to either the trustee or 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 U.S. dollars or foreign currencies or units based on or

relating to U.S. dollars or foreign currencies, including European Currency Units. 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;
- 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 United States 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 may 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 will be required to 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 will be 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 relating to such series contained 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 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 will 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 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 a 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 will provide 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 will have to deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange, and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we 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 behalf of, The Depository Trust Company or another depositary 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, will undertake 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 indicate otherwise in the applicable prospectus supplement, on any interest payment date, we will pay the interest on any debt securities to the person in whose name such 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, will we 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 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

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 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;
- 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 are to 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.

DESCRIPTION OF UNITS

We may issue units consisting of common stock, preferred stock, debt securities and/or warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. In this prospectus, we have summarized certain general features of the units. We urge you, however, to read the prospectus supplements related to the series of units being offered, as well as the unit agreements that contain the terms of the units. We will file as exhibits to an amendment to the registration statement of which this prospectus is a part, or will incorporate by reference from a current report on Form 8-K that we file with the SEC, as applicable, the form of unit agreement and any supplemental agreements that describe the terms of the series of units we are offering before the issuance of the related series of units.

We will evidence each series of units by unit certificates that we will issue under a separate agreement. We will enter into the unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

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

Anti-Takeover Provisions under Delaware law and our Delaware 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.

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.

Delaware statutory business combinations provision. We are subject to the anti-takeover provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a period of three years after the date of the transaction in which the person became an interested stockholder, unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. For purposes of Section 203, a "business combination" is defined broadly to include a merger, asset sale or other transaction resulting in a financial benefit to the interested stockholder, and, subject to certain exceptions, an "interested stockholder" is a person who, together with his or her affiliates and associates, owns (or within three years prior, did own) 15% or more of the 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.

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, as nearly equal in number as possible, serving staggered terms. Approximately one-third of our board will be elected each year. 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 and stockholder nominations of directors. Our restated bylaws provide that, for nominations to the board of directors or for other business to be properly brought by a stockholder before a meeting of stockholders, the stockholder must first have given timely notice of the proposal in writing to our Secretary. For an annual meeting, a stockholder's notice generally must be delivered not less than 45 days nor more than 75 days prior to the anniversary of the mailing date of the proxy statement for the previous year's annual meeting. Detailed requirements as to the form of the notice and information required in the notice are specified in the restated bylaws. If it is determined that business was not properly brought before a meeting in accordance with our restated bylaws, such business will not be conducted at the meeting. 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 directors.

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 directors.

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 provides that we will indemnify them to the fullest extent permitted by such law. We have also entered into indemnification agreements with our current and former directors and certain of our officers and key employees and expect to enter into a similar agreement with any new directors, officers or key employees.

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

The consolidated financial statements of Synta Pharmaceuticals Corp. as of December 31, 2007 and 2006, and for each of the years in the three-year period ended December 31, 2007, have been

incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

KPMG LLP's report includes a paragraph that states that the company adopted Statement of Financial Accounting Standard (SFAS) No. 123R, *Share-Based Payment*, effective January 1, 2006.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, 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 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. 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 exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in "Where to Find More Information." The documents we are incorporating by reference are:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2007 filed on March 20, 2008;
- our Current Report on Form 8-K filed on April 18, 2008;
- our Current Report on Form 8-K filed on April 29, 2008;
- the portions of our Definitive Proxy Statement on Schedule 14A filed on April 29, 2008 that are deemed "filed" with the SEC under the Exchange Act;
- our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2008 filed on May 14, 2008;

- our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2008 filed on August 7, 2008; and
- 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.

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

In addition, all documents subsequently filed by us pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act before the date any offering under this prospectus is terminated or completed are deemed to be incorporated by reference into, and to be a part of, this prospectus.

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.

We will provide without charge to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, upon the request of any such person, a copy of any or all of the information incorporated herein by reference (exclusive of exhibits to such documents unless such exhibits are specifically incorporated by reference herein). Requests, whether written or oral, for such copies should be directed to Secretary: 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.

5,555,556 Shares of Common Stock

PROSPECTUS SUPPLEMENT

Sole Book-Running Manager

LAZARD CAPITAL MARKETS

Co-Manager

RBC CAPITAL MARKETS

January 8, 2010