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FILED PURSUANT TO RULE 424(b)(5)
REGISTRATION NO. 333-176022

PROSPECTUS SUPPLEMENT
(to Prospectus dated August 19, 2011)

3,976,702 Shares of Common Stock

We are directly offering 3,976,702 shares to certain of our directors and entities affiliated with these directors.

Our common stock is listed on The NASDAQ Global Market under the symbol "SNTA." The last reported sale price of our common stock on July 25, 2012 was $6.48 per share.

Investing in our common stock involves a high degree of risk. Please read "Risk Factors" beginning on page S-11 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per share	Total
Sale price	$ 6.49	$ 25,808,795.98
Proceeds to Synta, before expenses	$ 6.49	$ 25,808,795.98

Delivery of the shares of common stock is expected to be made on or about July 27, 2012.

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Prospectus

ABOUT THIS PROSPECTUS SUPPLEMENT

On August 4, 2011, we filed with the Securities and Exchange Commission, or SEC, a registration statement on Form S-3 (File No. 333-176022) utilizing a shelf registration process relating to the securities described in this prospectus supplement, which registration statement became effective on August 19, 2011. Under this shelf registration process, we may, from time to time, sell common stock and other securities, including the securities to be sold in this offering.

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

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

statement in one of these documents is inconsistent with a statement in another document having a later date — for example, a document incorporated by reference in the accompanying prospectus — the statement in the document having the later date modifies or supersedes the earlier statement.

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

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

PROSPECTUS SUPPLEMENT SUMMARY

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

Overview

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

Oncology Programs

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

Ganetespib (Hsp90 Inhibitor)

Summary

Ganetespib is a novel, potent, small molecule inhibitor of heat shock protein 90 (Hsp90), a molecular chaperone which is required for the proper folding and activation of many cancer-promoting proteins. Inhibition of Hsp90 by ganetespib leads to the simultaneous degradation of many of its client proteins and the subsequent death or cell cycle arrest of cancer cells dependent on those proteins. A number of Hsp90 client proteins are also involved in the resistance of cancer cells to other anti-cancer treatments, such as chemotherapy. The ability to reduce cancer-cell drug resistance suggests the combination of ganetespib with chemotherapies or other agents may provide greater benefit than those agents administered alone. In preclinical studies, ganetespib has shown potent anti-cancer activity in a broad range of solid and hematologic cancers, both as a monotherapy and in combination with certain widely used anti-cancer agents.

Ganetespib is currently being evaluated in over 20 clinical trials, including trials evaluating monotherapy administration in certain genetically-defined targeted patient populations, such as our trials in ALK+ lung cancer, HER2+ breast cancer, and triple-negative breast cancer, as well as trials evaluating combination treatment in a broader patient population, such as our GALAXY lung cancer trial. The safety profile across these trials, involving over 600 patients treated with ganetespib to date, has been consistent and favorable. Ganetespib has shown no evidence of the serious liver or common ocular toxicities reported with other Hsp90 inhibitors, or the neurotoxicity, bone marrow toxicities, and alopecia characteristic of many chemotherapies. The most common adverse event reported with ganetespib has been transient, mild or moderate diarrhea, which can be prevented or effectively managed with standard supportive care.

In clinical trials, ganetespib has shown promising activity in a broad range of cancers, both as a monotherapy and in combination:

- *Monotherapy:*
    - Objective responses or anti-tumor activity have been seen in patients with ALK+ lung cancer, mutant BRAF lung cancer, mutant KRAS lung cancer, mutant KRAS gastric cancer, HER2+ breast cancer, triple-negative breast cancer, renal cancer, colorectal cancer, and melanoma.
- *Combination*: We recently announced encouraging interim results from our randomized, Phase 2b/3 GALAXY trial evaluating ganetespib plus docetaxel vs. docetaxel alone in second-line non-small cell lung cancer (NSCLC). Key findings from this interim analysis include:
    - Increases in progression-free survival (PFS), objective response rate, and disease control rate in patients treated with ganetespib. These increases were observed in patients with elevated lactate dehydrogenase (LDH) and patients with mutant KRAS, which are the two pre-specified co-primary endpoint populations, as well as in all adenocarcinoma patients
    - An encouraging improvement in overall survival (OS) in the all adenocarcinoma population
    - A profile suggestive of anti-angiogenic activity, consistent with preclinical results showing that ganetespib potently inhibits the hypoxia-induced factor (HIF) pathway that drives VEGF production in tumors. This includes: (a) enhanced activity in patients with elevated markers of tumor hypoxia (LDH), (b) favorable results in patients with adenocarcinoma histology, and (c) lack of benefit in patients with squamous cell histology, with possible safety concerns, including risk of bleeding, e.g. hemoptysis. This profile is consistent with known anti-angiogenic agents, e.g. direct VEGF inhibitors.
    - Favorable safety of the ganetespib plus docetaxel combination in adenocarcinoma patients

The results observed with ganetespib monotherapy administration suggest promising potential for treating specific, targeted populations: patients with cancers driven by increased expression or mutations in genes encoding "strong" Hsp90 clients. This represents a sizable unmet need and commercial opportunity. Our CHIARA trial, for example, evaluates ganetespib in patients with ALK+ lung cancer. There are an estimated 40,000-70,000 new patients diagnosed worldwide each year with this cancer type. Our ENCHANT trial evaluates ganetespib in patients with HER2+ or triple-negative breast cancer. Each of these subpopulations is estimated at 15-20% of the 1.4 million patients diagnosed with breast cancer worldwide each year.

The results observed to date in our GALAXY trial suggest an even broader unmet need and commercial opportunity for the combination therapy approach. An estimated 600,000 patients worldwide die each year from NSCLC with adenocarcinoma histology, the patient population being evaluated in our GALAXY trial. In addition, over 500,000 patients receive taxanes each year, across all cancer indications. The ability to combine with taxanes with minimal additional toxicity and possible enhanced activity represents a promising opportunity not only in lung cancer but in breast, prostate, ovarian, gastric, bladder, and head and neck cancers as well. In preclinical models, ganetespib has shown ability to enhance the activity of a number of other widely used anti-cancer agents, in addition to the taxanes, including pemetrexed, gemcitabine, bevacizumab, cytarabine, irinotecan, etoposide, doxorubicin, carboplatin, cisplatin, vincristine, tamoxifen, fulvestrant, temsirolimus, lapatinib, crizotinib, vemurafenib, selumetinib, and bortezomib. Combination trials with a number of these agents have recently been initiated or are planned for later this year.

Ganetespib Mechanism of Action and Preclinical Results

Ganetespib is a novel, small-molecule inhibitor of Hsp90 structurally unrelated to first-generation, ansamycin-family compounds, such as 17-AAG or 17-DMAG. In preclinical studies, ganetespib has shown 10-100 times greater potency than 17-AAG across a broad range of cancer cell types as well as activity in animal models that are resistant to treatment with 17-AAG.

Hsp90 is a molecular chaperone required for the proper folding and activation of many cancer-promoting proteins. Many of the client proteins of Hsp90, such as ALK, AKT, BCR-ABL, BRAF, KIT, MET, EGFR, FLT3, HER2, HIF-1alpha, PDGFRA, and VEGFR, are the targets of clinically validated cancer drugs such as Avastin, Erbitux, Gleevec, Herceptin, Nexavar, Sutent, Tarceva, Votrient, Xalkori, and Zelboraf. In preclinical studies, inhibition of Hsp90 by ganetespib results in simultaneous degradation of these client proteins, resulting in cancer cell death or cell cycle arrest.

Ganetespib also inhibits known mechanisms by which cancer cells evade or recover from other anti-cancer treatments. For example, cancer cells can evade DNA damage caused by chemotherapy or radiation therapy through modification of cell cycle dynamics and activation of DNA repair processes. Many of the cell cycle and DNA repair components — such as ATM, ATR, CHK1, BRCA1, and WEE1 — are Hsp90 client proteins. Ganetespib has shown activity both as a monotherapy and in combination in a broad range of *in vitro* and *in vivo* models of cancer. Combination activity has been observed in models of ALK+ NSCLC with Xalkori, KRAS mutant NSCLC with docetaxel, EGFR mutant NSCLC with Avastin, HER2+ breast cancer with Tykerb, colorectal cancer with radiation or platinum therapy, BRAF mutant melanoma with Zelboraf, hormone refractory prostate cancer with mTOR inhibitors, and AML with cytarabine.

Results published in *Molecular Cancer Therapeutics* in December 2011 highlighted certain physicochemical properties of ganetespib believed to contribute to its improved safety and activity relative to other Hsp90 inhibitors. These include smaller size, greater potency, improved ability to passively enter cells, improved interaction with the drug target, absence of a molecular component known to cause liver toxicity, and ability to penetrate deep into tumor tissues.

Results presented at the AACR-EORTC-NCI meeting in November 2011 and at the American Society of Clinical Oncology (ASCO) meeting in June 2012 demonstrated that common ocular toxicities seen with some Hsp90 inhibitors, but not observed in clinical trials with ganetespib or with 17-AAG, are associated with physicochemical properties that affect drug distribution to the eye.

Ganetespib Clinical Trials

Ganetespib is being evaluated in over 20 clinical trials ongoing, currently initiating, or recently completed, including trials in lung, breast, colon, gastric, prostate, melanoma, and pancreatic cancers, as well as in certain types of blood cancers. Many of these trials are sponsored by individual investigators or groups of investigators. We are sponsoring three principal trials evaluating ganetespib activity:

- GALAXY: a randomized Phase 2b/3 trial evaluating ganetespib in combination with docetaxel versus docetaxel alone as second-line therapy in patients with advanced NSCLC (Ganetespib Assessment in Lung cAncer with docetaXel);

- CHIARA: a Phase 2 trial evaluating ganetespib monotherapy in patients whose tumors have a genetic profile characterized by rearrangement of the ALK gene (ALK+) (Chaperone Inhibition in ALK Rearranged lung cAncer), and

- ENCHANT: a Phase 2 trial evaluating ganetespib monotherapy in patients with newly diagnosed HER2+ and triple-negative metastatic breast cancer (EvaluatiNg Chaperone inhibition by gANetespib in breasT cancer)

Ganetespib in combination with chemotherapy: the GALAXY Trial

Cancer treatments are often given in combination in order to maximize benefit to patients. A challenge with combination therapy is that the added toxicities from combining two or more potent anti-cancer agents may not be tolerable, particularly if the toxicity profiles from distinct treatments overlap. The favorable safety profile seen to date with ganetespib and the non-overlapping toxicities with many standard-of-care agents support such a combination therapy approach.

Results to date suggest potential for combining ganetespib and taxanes. These include a strong scientific rationale based on multiple mechanisms of synergistic anti-cancer activity, strong synergestic results in *in vitro* and *in vivo* experiments, and the encouraging safety profile seen in our Phase 1 combination study of ganetespib and docetaxel.

GALAXY Trial Design

In 2011 we initiated the GALAXY trial, a Phase 2b/3 program in patients with advanced NSCLC who have received one prior treatment for advanced disease, i.e., a second-line treatment setting. The GALAXY trial compares treatment with docetaxel alone, which is approved for second-line treatment, versus treatment with ganetespib plus docetaxel. The first stage, Phase 2b portion is designed to establish the clinical benefit and safety profile of ganetespib in combination with docetaxel relative to docetaxel alone, and to identify the patient populations, by biomarker or other disease characteristics, which may be most responsive to combination treatment. The first stage of this program is intended to build the clinical and operational experience needed to optimize the design and execution of the second stage, Phase 3 portion.

Patients in both arms receive a standard regimen of docetaxel 75 mg/m2 on day 1 of a 21-day cycle. Patients in the combination arm also receive ganetespib 150 mg/m2 on days 1 and 15. Treatment continues until disease progression per Response Evaluation Criteria in Solid Tumors (RECIST) criteria. Enrollment is stratified by ECOG performance status, LDH, smoking status, and time since diagnosis of metastatic disease to ensure balance of these prognostic factors between the two arms.

The Phase 2b portion of the trial was designed to enroll 240 second-line NSCLC patients, without selecting for specific biomarkers, in order to evaluate several pre-specified hypotheses on which patients might be most responsive to combination treatment. On initial design the co-primary endpoints were progression-free survival in all patients (the ITT or intent-to-treat population) and overall survival in patients with elevated baseline level of serum LDH. Several months after trial initiation, but before any substantial patient enrollment, the trial was amended to elevate improvement in progression-free survival in patients with mutant KRAS (the mKRAS population) from a secondary endpoint to a co-primary endpoint, based on clinical results observed in a separate ganetespib trial around that time. Both LDH and mutant KRAS were pre-specified for evaluation from blood and tumor tissue, respectively, by an independent, central laboratory.

Enhanced activity in the elevated LDH population was chosen as a primary hypothesis because an isoform of LDH is a marker of lack of oxygen, or hypoxia, in a tumor. Under low oxygen conditions, hypoxia-induced factor (HIF-1alpha) rises in cancer cells and has been shown in preclinical studies to increase tumor metastasis, angiogenesis, and resistance to chemotherapy. Inhibition of HIF-1alpha has been shown in preclinical studies to reduce metastases, improve survival, and enhance the anti-cancer activity of chemotherapy. Because ganetespib potently suppresses HIF-1alpha, which is an Hsp90 client protein, it was proposed that patients with elevated levels of baseline LDH might show enhanced benefit from ganetespib treatment. Recent trials with other agents whose activity depends on tumor oxygen state, including VEGF and mTOR inhibitors, have shown a correlation of activity with serum LDH levels, further supporting this hypothesis. Generally, one quarter to one third of patients in comparable trials present with elevated baseline levels of LDH.

Enhanced activity in the mutant KRAS population was chosen as a primary hypothesis based on both the known Hsp90 dependence of pathways active in this type of lung cancer and observations from other Synta trials. In a Phase 2 trial evaluating ganetespib monotherapy in lung cancer, as reported at the ASCO June 2011 meeting, approximately two thirds of patients with mutant KRAS showed tumor shrinkage following ganetespib treatment. In addition, in an investigator-sponsored Phase 2 trial in patients with esophagogastric cancer, a patient with mutant KRAS gastric cancer experienced a complete response following treatment with ganetespib monotherapy. The patient recently entered the 23rd month of treatment with ganetespib. Approximately 15% to 30% of NSCLC patients are estimated to have tumors with KRAS mutation.

The GALAXY trial was designed to enroll patients with all histologies — including both adenocarcinoma and squamous cell. Earlier this year enrollment of patients with squamous cell histology was terminated based on the lack of benefit observed in patients with this histology; possible safety concerns, including risk of bleeding; and the consistency of the emerging ganetespib profile with known anti-angiogenic agents, for which patients with squamous cell histology are commonly excluded from clinical trials or labeled indications. The trial was amended at that time to enroll a total of 240 patients with adenocarcinoma histology only.

The current co-primary endpoints of the first-stage, Phase 2b portion are: PFS in patients with elevated LDH and PFS in patients with mutant KRAS. Key secondary endpoints, to be evaluated with the statistical gatekeeping methodology, include OS and PFS in the all adenocarcinoma population. The Phase 2b stage is 90% powered to detect a PFS improvement from 6 to 12 weeks in patients with elevated LDH and from 5 weeks to 10 weeks in patients with mutant KRAS. For all adenocarcinoma patients, GALAXY is 88% powered to detect an improvement in PFS from 3 to 4.5 months, and 73% powered to detect an improvement in OS from 6 to 8.5 months. All powering assumptions are based on a 1-sided alpha of 0.05.

GALAXY Interim Results

In June 2012 we reported top line results from a planned interim analysis of the GALAXY trial. The analysis was planned for when approximately 50% of patients had been enrolled and had sufficient follow up, defined as one post-baseline scan. At the time of this analysis, completed in June, a total of 114 adenocarcinoma and 69 non-adenocarcinoma patients had been enrolled.

The table below lists primary and key secondary endpoints relating to the two co-primary patient populations, as well as the all adenocarcinoma population. At the time of the interim analysis, there were 31 patients identified as elevated LDH, and 20 patients as mutant KRAS. Of 73 adenocarcinoma samples successfully evaluated for KRAS status by the time of this analysis, 53 and 20 were identified as wild-type and mutant KRAS, respectively. Of the elevated LDH and mutant KRAS groups, 9 patients were positive for both markers. Responses were assessed per RECIST 1.1 criteria; there have been no complete responses seen in this trial. Results reported are for adenocarcinoma patients only.

Outcomes of GALAXY subgroups from the June interim analysis

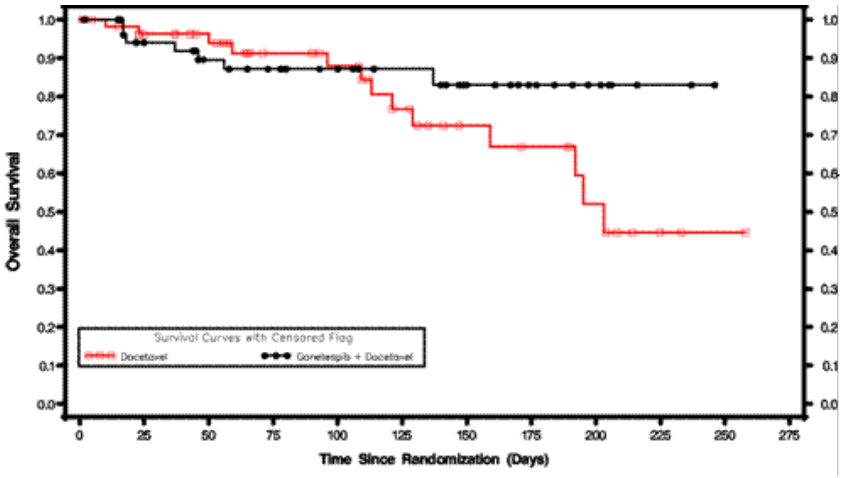
	Elevated LDH (N=31)		**Mutant KRAS (N=20)**		**All adeno (N=114)**	
	D (N=15)	**G+D (N=16)**	**D (N=11)**	**G+D (N=9)**	**D (N=59)**	**G+D (N=55)**
Primary endpoint						
median PFS	1.4 mo	4.2 mo	1.6 mo	4.2 mo	2.9 mo	4.2 mo
PRs (%)	0	2 (13)	1 (9)	2 (22)	5 (8)	8 (15)
Number of events						
# PFS events	12	8	5	3	31	23
# deaths	6	4	2	1	13	7

G: ganetespib, D: docetaxel
PR: partial response

These results are encouraging and consistent with the pre-specified hypotheses of enhanced activity in both the elevated LDH and the mutant KRAS populations.

We also reported interim OS results. Below is a Kaplan-Meier analysis of survival events in the all adenocarcinoma population. The Y-axis represents the fraction of patients alive in each arm of the study.

Overall survival in the GALAXY all adenocarcinoma population at the June interim analysis



Additional details will be provided at an upcoming medical meeting.

The adverse event profile has been comparable between both arms of the GALAXY trial. The proportion of adenocarcinoma patients with at least one adverse event (AE) was 64% vs. 82%; with grade 3 or greater AEs was 32% vs. 36%; with AEs leading to treatment discontinuation was 7% vs. 9%; and with AEs with outcome of death were 5.1% vs. 5.5%, for D (N=59) vs. G+D (N=55), respectively. The most common AEs, all grades were neutropenia (48% vs. 44%), diarrhea (10% vs. 40%) and fatigue (19% vs. 26%), for D vs. G+D, respectively. Diarrhea and fatigue were predominantly grade 1 and grade 2; the incidence of grade 3 or greater diarrhea was 0% vs. 2% and grade 3 or greater fatigue was 3% vs. 0% in D vs. G+D, respectively. The most common grade 3 or greater AEs were neutropenia (29% vs. 33%), leukopenia (5% vs. 4%), and nausea (3% vs. 4%). Trials with some other Hsp90 inhibitors have reported a high incidence of ocular toxicities. In this trial, there has been one report of an ocular-related adverse event (grade 2, transient blurred vision) in the G+D arm (2%) vs. no reports in the D arm.

Summary of GALAXY Trial Findings and Near-Term Plans

Key findings from the recent interim analysis include:

- Increases in PFS, objective response rate, and disease control rate in patients treated with ganetespib across the three major patient populations of interest: elevated LDH, mutant KRAS, and all adenocarcinoma patients. This activity was enhanced in the pre-specified biomarker groups, consistent with the preclinical and clinical rationale
- Encouraging improvement in OS in the all adenocarcinoma population
- A profile suggestive of anti-angiogenic activity, consistent with preclinical results showing that ganetespib potently inhibits the hypoxia-induced factor (HIF) pathway that drives VEGF production in tumors. This includes: (a) enhanced activity in patients with elevated markers of tumor hypoxia (LDH), (b) favorable results in patients with adenocarcinoma histology, and (c) lack of benefit in patients with squamous cell histology, with possible safety concerns, including risk of bleeding, e.g. hemoptysis.
- Favorable safety of the ganetespib plus docetaxel combination in adenocarcinoma patients

Our near term plans for the GALAXY program include:

- Conduct the next planned interim analysis and present these results at an upcoming medical meeting
- Meet with regulatory agencies, review the interim results, and discuss plans for the Phase 3 portion of the trial later this year
- Complete enrollment and transition to the Phase 3 portion of the trial later this year

Based on our current plans and projections, we anticipate final data from the Phase 2b portion of the trial in the first half of 2013, and final data from the Phase 3 portion in the first half of 2014.

Ganetespib as Monotherapy

ALK+ NSCLC: In June and July 2011 we presented results from a Phase 2 trial of ganetespib administered as a monotherapy in patients with advanced NSCLC at the ASCO Annual Meeting and the International Association for the Study of Lung Cancer (IASLC) 14th World Conference on Lung Cancer, respectively. Patients in this trial had failed to respond to, or experienced disease progression following, numerous prior therapies. In this trial, as in other trials, ganetespib treatment was associated with favorable safety.

Encouraging evidence of clinical activity was also observed in this trial, as evident by the durable objective tumor responses achieved in certain patients, as evaluated by RECIST. The disease control rate, using the standard definition of complete response plus partial response plus stable disease, was 54%. This rate compares favorably with disease control rates observed in trials for approved and experimental agents in a similar broad, pre-treated, advanced NSCLC patient population.

Results presented at these meetings also showed a connection between single-agent ganetespib clinical activity and certain tumor genetic profiles. Four of eight patients who were ALK+, i.e., for whom tumor genetic testing revealed rearrangements in the ALK gene, experienced confirmed partial responses following treatment with ganetespib (a 50% objective response rate, using the standard definition of complete response plus partial response). These responses were durable, with the responding patients remaining on therapy an average of about one year (range 7 to >21 months). Six of these eight patients experienced tumor shrinkage in target lesions, and seven of these eight patients (88%) achieved disease control for eight weeks or more. These results are encouraging when compared to results typically seen with chemotherapy and other agents in these advanced NSCLC treatment settings, for which objective response rates have been in the range of 5-10%.

Although only eight critzonib-untreated, ALK+ patients were reported in this trial, these results are comparable to those seen with the direct ALK inhibitor Xalkori® (crizotinib), which was granted accelerated approval in August 2011 by the FDA for the treatment of ALK+ NSCLC. In a Phase 1 trial enrolling 136 ALK+ patients and in a single-arm Phase 2 trial in 119 ALK+ patients , crizotinib demonstrated a 50% and a 61% objective response rate, respectively, by investigator review, and a 42% and 51% objective response rate, respectively, by independent review.

Ganetespib has also been shown to be active as monotherapy and in combination with crizotinib in preclinical models of ALK+ NSCLC. Importantly, ALK inhibition via direct inhibition of Hsp90 supports a complementary, rather than competitive, mechanism with crizotinib and other direct ALK inhibitors. Combined with clinical observations so far, these results present strong evidence that Hsp90 inhibition with ganetespib is a promising approach for treating ALK+ NSCLC patients.

To further characterize ganetespib activity in this treatment setting, we recently initiated the CHIARA trial to evaluate ganetespib monotherapy in ALK+ NSCLC patients who have not been previously treated with a direct ALK inhibitor. We expect preliminary results from this trial by the end of the year. In addition to CHIARA, a number of cancer centers and cooperative groups have approached us with proposals to support trials evaluating ganetespib in combination with other agents in ALK+ disease. An investigator-sponsored Phase 1/2 trial evaluating ganetespib and crizotinib combinations in ALK+ patients began enrolling patients at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City earlier this year.

HER2+ and triple negative metastatic breast cancer: At the San Antonio Breast Cancer Symposium in December 2011, researchers from MSKCC presented results from a Phase 2 trial evaluating ganetespib monotherapy in patients with metastatic breast canc\er who had been previously treated with multiple lines of chemotherapy or other anti-cancer agents. Results showed that 15% (2/13) of the HER2+ patients experienced a confirmed partial response and an additional 46% (6/13) achieved stable disease. These results with ganetespib in HER2+ disease are consistent with results from an earlier Phase 2 study of 17-AAG, a first-generation Hsp90 inhibitor, in patients who had progressed following treatment with one line of trastuzumab (Herceptin). In that trial 22% (6/27) of patients achieved a partial response and an additional 37% (10/27) achieved stable disease. While in the latter study 17-AAG was given in combination with trastuzumab, in the former study ganetespib was given as a monotherapy. Together, these studies present strong evidence that Hsp90 inhibition is a promising approach for treating HER2+ breast cancer.

Results with ganetespib in patients with triple-negative breast cancer (TNBC) were also reported in December 2011. One of three evaluable patients in the Phase 2 clinical trial experienced significant tumor shrinkage following three doses of ganetespib. An objective response was also reported in a patient with TNBC participating in a ganetespib Phase 1 trial. TNBC represents a difficult-to-treat disease, for which no targeted therapies are currently approved. These results are encouraging, and suggest that ganetespib is active in TNBC.

We recently initiated the ENCHANT trial designed to evaluate ganetespib monotherapy as first-line treatment for both metastatic HER2+ breast cancer and TNBC. In addition, MSKCC has announced that it will initiate a Phase 1/2 trial evaluating

ganetespib in combination with paclitaxel and Herceptin in HER2+ breast cancer, and ganetespib in combination with paclitaxel in TNBC.

Additional oncology indications

In addition to the clinical trials we plan to initiate and continue in 2012, a number of ganetespib trials sponsored by third parties, including cooperative groups, foundations, and individual investigators, have recently initiated or are expected to initiate in 2012. These include

- the trials evaluating ganetespib in breast cancer and in ALK+ lung cancer sponsored by MSKCC described above
- a randomized trial evaluating the combination of fulvestrant and ganetespib in patients with hormone receptor-positive, metastatic breast cancer, being conducted at the Dana-Farber Cancer Institute, which began enrolling patients earlier this year
- a trial evaluating the combination of ganetespib with capecitabine and radiation in patients with locally advanced rectal cancer being conducted at Emory University, which began enrolling patients earlier this year
- a trial evaluating both ganetespib monotherapy and the combination of ganetespib and bortezomib in multiple myeloma, supported by a grant of up to $1 million by the Multiple Myeloma Research Foundation, which began enrolling patients earlier this year
- a trial evaluating ganetespib in combination with pemetrexed and cisplatin in patients with malignant pleural mesothelioma, being sponsored by Cancer Research UK, which is expected to initiate later this year
- a randomized trial evaluating the combination of ganetespib and the chemotherapy drug ara-C in elderly patients with acute myeloid leukemia (AML)

Additional ongoing investigator-sponsored trials include trials in prostate cancer, pancreatic cancer, liver cancer, melanoma, and ocular melanoma.

Elesclomol (Mitochondria-Targeting Agent)

Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death (apoptosis) in cancer cells through a novel mechanism: disrupting cancer cell mitochondrial metabolism. In preclinical experiments, anti-cancer activity of elesclomol has been shown to correlate with certain biomarkers, including LDH, which can distinguish between active mitochondria (sufficient oxygen) and inactive mitochondria (insufficient oxygen). Consistent with these findings in three randomized clinical trials, LDH was an important predictor of elesclomol treatment outcome.

Our current clinical program for elesclomol includes a clinical trial of elesclomol as a monotherapy in AML. In December 2009, we presented results at the American Society for Hematology (ASH) meeting showing that elesclomol was highly active against AML cell lines and primary blast cells from AML patients. In February 2011, we announced that the first patient had been treated in a Phase 1 dose escalation study of elesclomol as a single agent in patients with AML. This trial will enroll up to 36 patients with relapsed or refractory AML and total baseline serum LDH level less than 0.8 times ULN. Patients will be treated with elesclomol sodium on a once-weekly schedule at a starting dose of 200 mg/m2, with dose escalation planned based on safety, tolerability and pharmacokinetic considerations. The trial is being conducted at Princess Margaret Hospital in Toronto, Canada and at MSKCC in New York.

We are also evaluating the use of elesclomol in combination with paclitaxel in ovarian cancer. In March 2011, the Gynecological Oncology Group (GOG), initiated a Phase 2 clinical trial of elesclomol in combination with paclitaxel for the treatment of persistent or recurrent ovarian, fallopian tube or primary peritoneal cancer for patients with total baseline serum LDH level less than 0.8 times ULN. The GOG is a non-profit organization with the purpose of promoting excellence in the quality and integrity of clinical and basic scientific research in the field of gynecologic malignancies. The National Cancer Institute is providing financial support of up to approximately $300,000 for the trial through its Cancer Therapy Evaluation Program.

STA-9584 (Vascular Disrupting Agent)

STA-9584 is a novel, injectable, small molecule compound that appears to disrupt the blood vessels that supply tumors with oxygen and essential nutrients, and is in preclinical development. In March 2011, we received a $1 million grant from the United States Department of Defense (DoD) for the development of STA-9584 in advanced prostate cancer.

Inflammatory Disease Programs

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

CRACM Ion Channel Inhibitors

We have developed novel, small molecule inhibitors of CRACM ion channels expressed on immune cells. Our CRACM ion channel inhibitors have shown 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 (RA), asthma, chronic obstructive pulmonary disease (COPD), allergy, transplant rejection, and other autoimmune diseases and inflammatory conditions. We have several promising CRACM inhibitors in preclinical development. Because there are a number of CRACM ion channel targets on immune cells, we believe that CRACM inhibitor compounds can be developed that target different diseases.

Roche CRACM Inhibitor Alliance

In December 2008, as amended in February 2010, February 2011 and July 2011, we formed a strategic alliance with Roche to discover, develop, and commercialize small-molecule drugs targeting CRACM channels, which we refer to as the Roche Agreement. The goal of this alliance was to develop a novel category of oral, disease-modifying agents for the treatment of RA and other autoimmune diseases and inflammatory conditions. The Roche Agreement was terminated by Roche effective on February 16, 2012.

As a result of termination of the Roche Agreement, the research, development and commercialization licenses granted to Roche by us have terminated. Ownership of all rights to all Licensed Compounds (as defined in the agreement) (including the scientific data relating to those compounds) has reverted to us. We have also received an exclusive license to use Roche's patent rights and know-how to research, develop, manufacture, commercialize and import any collaboration compound, including the Licensed Compounds. We are obligated to pay a low single digit royalty on a country-by-country and Licensed Product-by-Licensed Product (as defined in the agreement) basis upon commercialization of any Licensed Product.

IL-12/23 Inhibitors

We have identified several small molecule IL-12/23 inhibitors that represent a promising opportunity to develop drug candidates that could be administered orally and potentially address a wide range of serious inflammatory diseases with high unmet medical needs.

Company 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 or the accompanying prospectus. We have included our website address as a factual reference and do not intend it to be an active link to our website. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and all amendments to those reports, are available free of charge through the "Investors—SEC Filings" section of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC.

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

The Offering

Common stock offered by us	3,976,702 shares
Common stock to be outstanding after this offering	61,789,657 shares
Use of proceeds	We intend to use the net proceeds from this offering for general corporate purposes, which may include research and development expenditures, clinical trial expenditures, manufacture and supply of drug substance and drug products, acquisitions of new technologies, capital expenditures and working capital. See "Use of Proceeds" on page S-12 of this prospectus supplement.
Risk factors	Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page S-11 of the accompanying prospectus.
NASDAQ Global Market symbol	SNTA

The number of shares to be outstanding after this offering is based on 57,812,955 shares of common stock outstanding as of June 30, 2012. It does not include:

- 6,161,179 shares of our common stock issuable upon exercise of stock options outstanding as of June 30, 2012 under our stock option plans as of that date, at a weighted average exercise price of $7.01 per share; and
- 2,327,381 shares of our common stock available as of June 30, 2012 for future grant or issuance pursuant to our stock-based plan for employees, directors and consultants.

RISK FACTORS

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks discussed under the section captioned "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2011, as filed with the SEC on February 22, 2012, which is incorporated by reference in the prospectus supplement and the accompanying prospectus in their entirety, together with other information in this prospectus supplement, the accompanying prospectus and the information and documents incorporated by reference. If any of these risks actually occurs, our business, financial condition, results of operation or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents we have filed with the SEC that are incorporated by reference contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to, statements about:

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

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading "Risk Factors" on page S-11 of this prospectus supplement and in our SEC filings. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement.

You should read this prospectus supplement, the accompanying prospectus and the documents we have filed with the SEC that are incorporated by reference completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements.

USE OF PROCEEDS

The net proceeds from the sale of all 3,976,702 shares in this offering are estimated to be approximately $25.8 million, after deducting estimated offering expenses payable by us.

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

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

DILUTION

Our net tangible book value at March 31, 2012 was $33.8 million, or $0.59 per share. We calculate net tangible book value per share by subtracting our total liabilities from our total tangible assets and dividing the difference by the number of outstanding shares of our common stock. After giving effect to the sale of 3,976,702 shares of common stock at the sale price of $6.49 per share, less the estimated offering expenses payable by us, our as adjusted net tangible book value at March 31, 2012 would be $59.5 million, or $0.97 per share. This represents an immediate increase in the as adjusted net tangible book value of $0.38 per share to existing stockholders and an immediate dilution of $5.52 per share to investors participating in this offering. The following table illustrates this per share dilution:

Sale price per share			$	6.49
Net tangible book value per share as of March 31, 2012	$	0.59		
Increase per share attributable to this offering	$	0.38		
As adjusted net tangible book value per share after this offering			$	0.97
Dilution per share to investors participating in this offering			$	5.52

The information above does not include:

- 6,813,101 shares of our common stock issuable upon exercise of stock options outstanding as of March 31, 2012 under our stock option plans as of that date, at a weighted average exercise price of $6.98 per share; and
- 1,969,531 shares of our common stock available as of March 31, 2012 for future grant or issuance pursuant to our stock-based plan for employees, directors and consultants.

PRICE RANGE OF COMMON STOCK

Our common stock is listed on The NASDAQ Global Market under the symbol "SNTA." The last reported sale price for our common stock on July 25, 2012 was $6.48 per share. The table below sets forth closing information on the range of high and low sales prices for our common stock during the periods indicated.

	High	Low
Fiscal Year ended December 31, 2010		
First Quarter	$ 6.50	$ 3.81
Second Quarter	4.79	2.66
Third Quarter	4.13	2.55
Fourth Quarter	6.50	3.23
Fiscal Year ended December 31, 2011		
First Quarter	$ 6.93	$ 4.26
Second Quarter	6.27	4.30
Third Quarter	5.23	3.25
Fourth Quarter	5.15	3.02
Fiscal Year ending December 31, 2012		
First Quarter	$ 5.74	$ 4.03
Second Quarter	$ 8.50	$ 3.57
Third Quarter (through July 25, 2012)	$ 7.00	$ 5.35

DIVIDEND POLICY

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

PLAN OF DISTRIBUTION

We are directly selling 3,976,702 shares of common stock to certain of our directors and entities affiliated with these directors.

Bruce Kovner, one of our directors and our largest stockholder who beneficially owns approximately 26.1% of our outstanding shares of common stock prior to this offering, will purchase 3,081,664 shares of our common stock directly from us in this offering. Upon completion of this offering, Mr. Kovner will beneficially own approximately 29.4% of our outstanding shares of common stock.

Wyandanch Partners, L.P., which is controlled by Keith R. Gollust, one of our directors who beneficially owns approximately 3.7% of our outstanding shares of common stock prior to this offering, will purchase 770,416 shares of our common stock directly from us in this offering. Upon completion of this offering, Mr. Gollust will beneficially own approximately 4.7% of our outstanding shares of common stock.

Robert N. Wilson, one of our directors who beneficially owns approximately 1.1% of our outstanding shares of common stock prior to this offering, will purchase 100,000 shares of our common stock directly from us in this offering. Upon completion of this offering, Mr. Wilson will beneficially own approximately 1.2% of our outstanding shares of common stock.

Donald W. Kufe, one of our directors who beneficially owns less than 1% of our outstanding shares of common stock prior to this offering, will purchase 4,622 shares of our common stock directly from us in this offering. Upon completion of this offering, Dr. Kufe will continue to beneficially own less than 1% of our outstanding shares of common stock.

Safi R. Bahcall, Ph.D., our President and Chief Executive Office and one of our directors who beneficially owns approximately 5.0% of our outstanding shares of common stock prior to this offering, will purchase 20,000 shares of our common stock directly from us in this offering. Upon completion of this offering, Dr. Bahcall will beneficially own approximately 4.7% of our outstanding shares of common stock.

The shares were offered directly to the directors and affiliated entities without a placement agent, underwriter, broker or dealer. In order to comply with certain rules and regulations of The NASDAQ Stock Market LLC, the shares will be sold at a price per share of $6.49, which was the consolidated closing bid price of our common stock as reported on The NASDAQ Global Market on July 25, 2012.

We estimate that the total expenses of this offering payable by us, will be about $50,000.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts.

EXPERTS

The consolidated financial statements of Synta Pharmaceuticals Corp. appearing in its Annual Report (Form 10-K) for the year ended December 31, 2011, and the effectiveness of Synta's internal control over financial reporting as of December 31, 2011 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's website at *http://www.sec.gov*.

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

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

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" information from other documents that we file with them, which means that we can disclose important information in this prospectus supplement by referring to those documents. The information incorporated by reference is considered to be part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede the information in this prospectus supplement. We incorporate by reference the following documents (unless otherwise noted, the SEC file number for each of the documents listed below is 001-33277):

- our Annual Report on Form 10-K, for the fiscal year ended December 31, 2011, filed with the SEC on February 22, 2012;
- our Quarterly Report on Form 10-Q, for the quarter ended March 31, 2012, filed with the SEC on May 3, 2012;

- our Current Reports on Form 8-K filed on January 6, 2012, January 11, 2012, January 26, 2012, February 15, 2012, April 5, 2012, June 19, 2012 and June 28, 2012 (Item 8.01 only);

- the portions of our Definitive Proxy Statement on Schedule 14A that are deemed "filed" with the SEC under the Securities Exchange Act of 1934, as amended, filed on April 27, 2012;

- the description of our common stock contained in our Registration Statement on Form 8-A filed on January 26, 2007, including any amendment or report filed for the purpose of updating such description; and

- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Securities Exchange Act of 1934, as amended, after the date of this prospectus supplement and prior to the termination of this offering shall be deemed to be incorporated by reference in this prospectus supplement and to be a part hereof from the date of filing such reports and other documents.

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

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PROSPECTUS

SYNTA PHARMACEUTICALS CORP.

$150,000,000
COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
RIGHTS
PURCHASE CONTRACTS
UNITS

This prospectus will allow us to issue, from time to time at prices and on terms to be determined at or prior to the time of the offering, up to $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 or exchange for the debt securities; common stock upon conversion of or exchange for the preferred stock; common stock, preferred stock or debt securities upon the exercise of warrants, rights or performance of purchase contracts; or any combination of these securities upon the performance of purchase contracts.

Of the $150,000,000 of our securities that we may issue, we may issue up to $35,000,000 of shares of our common stock, not to exceed 8,106,329 shares, to Azimuth Opportunity Ltd., or Azimuth, pursuant to a Common Stock Purchase Agreement between us and Azimuth dated October 4, 2010, which we refer to as the Azimuth Agreement. The offering price for shares sold pursuant to the Azimuth Agreement, net of discounts and commissions payable by us, will be at a discount of between 4.875% and 6.0% from the volume-weighted average price of our common stock at the time of sale, as reported on The NASDAQ Global Market. Upon each sale of our common stock to Azimuth under the Azimuth Agreement, we have also agreed to pay Reedland Capital Partners, an Institutional Division of Financial West Group, member FINRA/SIPC ("FWG/Reedland"), a placement agent commission equal to 1.0% of the aggregate dollar amount paid to us for the common stock purchased by Azimuth.

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

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

Section 2(a)(11) of the Securities Act of 1933, as amended, or the Securities Act, and any profits on the sales of shares of our common stock by Azimuth and any discounts, commissions or concessions received by Azimuth may be deemed to be underwriting discounts and commissions under the Securities Act. This prospectus and any accompanying prospectus supplement also cover the sale of these shares by Azimuth to the public.

Our common stock is listed on The Nasdaq Global Market under the symbol "SNTA." On August 18, 2011, the last reported sale price of our common stock was $3.86 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 3 of this prospectus under the caption "Risk Factors." We may include specific risk factors in supplements to this prospectus under the caption "Risk Factors." This prospectus may not be used to sell our securities unless accompanied by a prospectus supplement.

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

The date of this prospectus is August 19, 2011.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants, rights or purchase contracts to purchase any of such securities, either individually or in units, in one or more offerings, with a total value of up to $150,000,000, including up to $35,000,000 of shares of common stock that we may sell from time to time to Azimuth Opportunity Ltd., or Azimuth, pursuant to the Azimuth Agreement. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering.

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

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

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

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

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

PROSPECTUS SUMMARY

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

About Synta Pharmaceuticals Corp.

We are a biopharmaceutical company focused on discovering, developing, and commercializing small molecule drugs to extend and enhance the lives of patients with severe medical conditions, including cancer and chronic inflammatory diseases. We have two drug candidates in clinical trials for treating multiple types of cancer and several drug candidates in the preclinical stage of development. Each of our drug candidates was discovered and developed internally using our proprietary, unique chemical compound library and integrated discovery engine. We have granted Hoffman-La Roche an exclusive license to develop and commercialize certain compounds from our calcium release activated calcium modulator program resulting from our research partnership with them. We retain full ownership of all of our other drug candidates.

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.

Additional Information

Our principal executive offices are located at 45 Hartwell Avenue, Lexington, Massachusetts 02421, and our telephone number is (781) 274-8200. Our website address is www.syntapharma.com. The information contained on our website is not incorporated by reference into, and does not form any part of, this prospectus 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, without limitation, Synta Pharmaceuticals, our corporate logo and the GALAXY Trial. 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, rights or purchase contracts 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 the offering, of which up to $35,000,000 may be sold to Azimuth in shares of our common stock under the Azimuth Agreement, as described below. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

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

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

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

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

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

Offering of Shares of Common Stock Pursuant to the Azimuth Agreement

Pursuant to the Azimuth Agreement, Azimuth is committed to purchase and we may offer, from time to time and at our sole discretion, up to the lesser of (a) $35,000,000 of our common stock, or (b) 8,106,329 shares of common stock. The offering price for any shares sold pursuant to the Azimuth Agreement, net of discounts and commissions payable by us, will be at a discount of between 4.875% and 6.0% from the volume-weighted average price of our common stock at the time of sale, as reported on The NASDAQ Global Market. Upon each sale of our common stock to Azimuth under the Azimuth Agreement, we have also agreed to pay Reedland Capital Partners, an Institutional Division of Financial West Group, member FINRA/SIPC ("FWG/Reedland"), a placement agent commission equal to 1.0% of the aggregate dollar amount paid to us for the common stock purchased by Azimuth. As of the date of this prospectus, we have not sold any common stock to Azimuth under the Azimuth Agreement.

RISK FACTORS

Investing in our securities involves significant 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, as revised or supplemented by our subsequent quarterly reports on Form 10-Q or our current reports on Form 8-K on file with the SEC, all of which are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations.

RATIO OF EARNINGS TO FIXED CHARGES

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

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

USE OF PROCEEDS

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

PLAN OF DISTRIBUTION

General Plan of Distribution

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

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

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

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

If we utilize an underwriter in the sale of the securities being offered by this prospectus, we will execute an underwriting agreement with the underwriter at the time of sale, and we will provide the name of any underwriter in the prospectus supplement which the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we, or the purchasers of the securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions.

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

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

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

Shares of our common stock sold pursuant to the registration statement of which this prospectus is a part will be authorized for quotation and trading on The Nasdaq Global Market. The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on The Nasdaq Global Market or any

securities market or other securities exchange of the securities covered by the prospectus supplement. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

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

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

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

Plan of Distribution for Shares of Common Stock Sold Pursuant to the Azimuth Agreement

The Azimuth Agreement provides that, upon the terms and subject to the conditions set forth therein, Azimuth is committed to purchase from us up to $35.0 million worth of shares of our common stock over the 18-month term of the Azimuth Agreement; provided, however, that we may not sell more than 8,106,329 shares of our common stock, which is equal to one share less than 20% of our outstanding shares of common stock on the date of the Azimuth Agreement. From time to time over the term of the Azimuth Agreement, and at our sole discretion, we may present Azimuth with draw down notices requiring Azimuth to purchase a specified dollar amount of shares of our common stock, subject to certain limitations and so long as specified conditions are met. The price per share at which the shares will be sold, and therefore the number of shares to be sold pursuant to the draw down notice, is determined over a ten consecutive trading-day period, or such other period as is mutually agreed by Azimuth and us, referred to as the pricing period. We are able to present Azimuth with up to 24 draw down notices during the 18-month term of the Azimuth Agreement, with only one draw down per pricing period and a minimum of five trading days elapsing between each pricing period, unless otherwise mutually agreed by Azimuth and us. Each draw down is limited in size, unless otherwise mutually agreed by Azimuth and us, to the lesser of (i) certain agreed-upon draw down amounts (the largest of which is $4.25 million), based on the threshold price (discussed below) established by us for the draw down, and (ii) 2.5% of our market capitalization at the time of such draw down.

Once presented with a draw down notice, Azimuth is required to purchase a pro rata portion of the dollar amount of shares specified in the notice for each trading day during the pricing period on which the daily volume weighted average price for our common stock exceeds a threshold price specified by us in the draw down notice. The per share purchase price for the shares sold on any particular trading day during the pricing period will equal the daily volume weighted average price of our common stock for that day, less a discount ranging from 4.875% to 6%. The amount of the discount varies based on the threshold price specified by us. If the daily volume weighted average price of our common stock falls below the threshold price on any trading day during a pricing period, the Azimuth Agreement provides that Azimuth will not be required to purchase the pro rata portion of the dollar amount of shares of common stock allocated to that day. However, at its election, Azimuth may purchase the pro rata portion of the dollar amount of shares allocated to that day at the threshold price less the applicable discount described above. The total number of shares sold to Azimuth during each draw down will be the sum of the number of shares required and/or elected to be purchased on each day of the pricing period. The Azimuth Agreement also provides that from time to time, and at our sole discretion, we may grant Azimuth the option to purchase additional shares of our common stock up to an aggregate amount specified by us during each draw down pricing period. Upon Azimuth's exercise of such option, we would sell to Azimuth the shares of our common stock subject to such option at a price equal to the greater of the daily volume weighted average price of our common stock on the day Azimuth notifies us of its election to exercise its option or the threshold price for the option determined by us, less a discount calculated in the same manner as for the fixed amount set forth in the draw down notices.

Any sale of our shares of common stock to Azimuth will be registered on our registration statement of which this prospectus is a part, which also covers the sale of those shares from time to time by Azimuth to the public. Azimuth is an "underwriter" within the meaning of Section 2(a)(11) of the Securities Act.

Azimuth has informed us that it will use an unaffiliated broker-dealer to effectuate all sales, if any, of the common stock that it may purchase from us pursuant to the Azimuth Agreement. Such sales will be made on The NASDAQ Global Market at prices and at terms then prevailing or at prices related to the then current market price. Each such unaffiliated broker-dealer will be an underwriter within the meaning of Section 2(a)(11) of the Securities Act. Azimuth has informed us that each such broker-dealer will receive commissions from Azimuth that will not exceed customary brokerage commissions. In compliance with the guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus. We will pay the fees associated with a filing for the equity line of credit arrangement with the FINRA, and Azimuth will pay all other expenses associated with the sale of our common stock it acquires pursuant to the Azimuth Agreement.

The shares of common stock may be sold in one or more of the following manners:

- ordinary brokerage transactions and transactions in which the broker solicits purchasers; or
- a block trade in which the broker or dealer so engaged will attempt to sell the shares as agent, but may position and resell a portion of the block as principal to facilitate the transaction.

Azimuth has agreed that during the term of and for a period of 90 days after the termination of the Azimuth Agreement, neither Azimuth nor any of its affiliates will, directly or indirectly, sell any of our securities except the shares that it owns or has the right to purchase pursuant to the provisions of a draw down notice. Azimuth has agreed that during the periods listed above neither it nor any of its affiliates will enter into a short position with respect to shares of our common stock except that Azimuth may sell shares that it is obligated to purchase under a pending draw down notice but has not yet taken possession of so long as Azimuth covers any such sales with the shares purchased pursuant to such draw down notice. Azimuth has further agreed that during the periods listed above it will not grant any option to purchase or acquire any right to dispose or otherwise dispose for value of any shares of our common stock or any securities convertible into, or exchangeable for, or warrants to purchase, any shares of our common stock, or enter into any swap, hedge or other agreement that transfers, in whole or in part, the economic risk of ownership of our common stock, except for the sales permitted by the prior two sentences.

In addition, Azimuth and any unaffiliated broker-dealer will be subject to liability under the federal securities laws and must comply with the requirements of the Securities Act and the Securities Exchange Act of 1934, as amended, or the Exchange Act, including, without limitation, Rule 10b-5 and Regulation M under the Exchange Act. These rules and regulations may limit the timing of purchases and sales of shares of common stock by Azimuth or any unaffiliated broker-dealer. Under these rules and regulations, Azimuth and any unaffiliated broker-dealer:

- may not engage in any stabilization activity in connection with our securities;
- must furnish each broker which offers shares of our common stock covered by the prospectus that is a part of our registration statement with the number of copies of such prospectus and any prospectus supplement which are required by each broker; and
- may not bid for or purchase any of our securities or attempt to induce any person to purchase any of our securities other than as permitted under the Exchange Act.

These restrictions may affect the marketability of the shares of common stock by Azimuth and any unaffiliated broker-dealer.

We have agreed to indemnify and hold harmless Azimuth and each person who controls Azimuth against certain liabilities, including liabilities under the Securities Act. We have agreed to pay up to $35,000 of Azimuth's reasonable attorneys' fees and expenses (exclusive of disbursements and out-of-pocket expenses) incurred by Azimuth in connection with the preparation, negotiation, execution and delivery of the Azimuth Agreement and related transaction documentation. Further, we have agreed that if we issue a draw down notice and fail to deliver

the shares to Azimuth on the applicable settlement date, and such failure continues for ten trading days, we have agreed to pay Azimuth damages in cash or restricted shares of our common stock, at Azimuth's election. Azimuth has agreed to indemnify and hold harmless us and each of our directors, officers and persons who control us against certain liabilities, including liabilities under the Securities Act that may be based upon written information furnished by Azimuth to us for inclusion in this prospectus or any other prospectus or prospectus supplement related to the Azimuth Agreement.

Upon each sale of our common stock to Azimuth under the Azimuth Agreement, we have also agreed to pay FWG/Reedland, a placement fee equal to 1.0% of the aggregate dollar amount of common stock purchased by Azimuth. We have agreed to indemnify and hold harmless FWG/Reedland against certain liabilities, including liabilities under the Securities Act. We have agreed to pay up to $18,500 of FWG/Reedland's reasonable attorneys' fees and expenses incurred in connection with the preparation of any filings required to be made by FWG/Reedland in connection with the equity line of credit arrangement.

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, 2011, we had 49,495,023 shares of common stock outstanding and approximately 85 stockholders of record.

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

General

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

Transfer Agent and Registrar

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

Nasdaq Global Market

Our common stock is listed for quotation on The Nasdaq Global Market under the symbol “SNTA.”

DESCRIPTION OF PREFERRED STOCK

We are authorized to issue 5,000,000 shares of preferred stock, par value $0.0001 per share. As of August 19, 2011, no shares of our preferred stock were outstanding or designated. The following summary of certain provisions of our preferred stock does not purport to be complete. You should refer to our restated certificate of incorporation and our restated bylaws, both of which are included as exhibits to the registration statement of which this prospectus is a part. The summary below is also qualified by provisions of applicable law.

General

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

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

- the title and stated value;
- the number of shares offered, the liquidation preference, if any, per share and the purchase price;
- the dividend rate(s), period(s) and/or payment date(s), or method(s) of calculation for such dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption, if applicable;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated) and exchange period;
- voting rights, if any, of the preferred stock;
- a discussion of any material and/or special U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of the affairs of Synta; and
- any material limitations on issuance of any class or series of preferred stock ranking pari passu with or senior to the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of Synta.

Transfer Agent and Registrar

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

DESCRIPTION OF DEBT SECURITIES

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

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

The following summaries of material provisions of the senior debt securities, the subordinated debt securities and the indentures are subject to, and qualified in their entirety by reference to, all the provisions of the indenture applicable to a particular series of debt securities.

General

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

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

- the title or designation;
- the aggregate principal amount and any limit on the amount that may be issued;
- the currency or units based on or relating to currencies in which debt securities of such series are denominated and the currency or units in which principal or interest or both will or may be payable;
- whether we will issue the series of debt securities in global form, the terms of any global securities and who the depositary will be;
- the maturity date and the date or dates on which principal will be payable;
- the interest rate, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the date or dates interest will be payable and the record dates for interest payment dates or the method for determining such dates;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- the terms of the subordination of any series of subordinated debt;
- the place or places where payments will be payable;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;

- the date, if any, after which, and the price at which, we may, at our option, redeem the series of debt securities pursuant to any optional redemption provisions;
- the date, if any, on which, and the price at which we are obligated, pursuant to any mandatory sinking fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities;
- whether the indenture will restrict our ability to pay dividends, or will require us to maintain any asset ratios or reserves;
- whether we will be restricted from incurring any additional indebtedness;
- a discussion on any material or special U.S. federal income tax considerations applicable to a series of debt securities;
- the denominations in which we will issue the series of debt securities, if other than denominations of $1,000 and any integral multiple thereof; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities.

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

Conversion or Exchange Rights

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

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

The indentures do not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of all or substantially all of our assets. However, any successor to or acquirer of such assets must assume all of our obligations under the indentures or the debt securities, as appropriate.

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

Events of Default Under the Indenture

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

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

- if specified events of bankruptcy, insolvency or reorganization occur as to us.

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

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

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

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the debenture trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

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

- the holder previously has given written notice to the debenture trustee of a continuing event of default with respect to that series;
- the holders of at least a majority in aggregate principal amount of the outstanding debt securities of that series have made written request, and such holders have offered reasonable indemnity to the debenture trustee to institute the proceeding as trustee; and
- the debenture trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series (or at a meeting of holders of such series at which a quorum is present, the holders of a majority in principal amount of the debt securities of such series represented at such meeting) other conflicting directions within 60 days after the notice, request and offer.

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

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

Modification of Indenture; Waiver

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

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

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

- extending the fixed maturity of the series of debt securities;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or any premium payable upon the redemption of any debt securities;
- reducing the principal amount of discount securities payable upon acceleration of maturity;
- making the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment or waiver.

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

Discharge

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

- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

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

Form, Exchange, and Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we otherwise specify in the applicable prospectus supplement, in denominations of $1,000 and any integral multiple thereof. The indentures provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on 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, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the debenture trustee under such indenture must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the debenture trustee is under no obligation to exercise any of the powers given it by the indentures at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment and Paying Agents

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

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, 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

General

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

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

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the designation, amount and terms of the securities purchasable upon exercise of the warrants;
- if applicable, the exercise price for shares of our common stock and the number of shares of common stock to be received upon exercise of the warrants;
- if applicable, the exercise price for shares of our preferred stock, the number of shares of preferred stock to be received upon exercise, and a description of that series of our preferred stock;
- if applicable, the exercise price for our debt securities, the amount of debt securities to be received upon exercise, and a description of that series of debt securities;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- if applicable, the date from and after which the warrants and the common stock, preferred stock and/or debt securities will be separately transferable;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of the warrants, if any;
- any redemption or call provisions;
- whether the warrants may be sold separately or with other securities as parts of units; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

Transfer Agent and Registrar

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

DESCRIPTION OF RIGHTS

General

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

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

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

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

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

than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

Rights Agent

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

DESCRIPTION OF PURCHASE CONTRACTS

We may issue purchase contracts, including contracts obligating holders to purchase from us, and for us to sell to holders, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants or rights, or securities of an entity unaffiliated with us, or any combination of the above, at a future date or dates. Alternatively, the purchase contracts may obligate us to purchase from holders, and obligate holders to sell to us, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants, rights or other property, or any combination of the above. The price of the securities or other property subject to the purchase contracts may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula described in the purchase contracts. We may issue purchase contracts separately or as a part of units each consisting of a purchase contract and one or more of our other securities described in this prospectus or securities of third parties, including U.S. Treasury securities, securing the holder's obligations under the purchase contract. The purchase contracts may require us to make periodic payments to holders or vice versa and the payments may be unsecured or pre-funded on some basis. The purchase contracts may require holders to secure the holder's obligations in a manner specified in the applicable prospectus supplement.

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

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

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

DESCRIPTION OF UNITS

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

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

General

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

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

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

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

Unit Agent

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

Issuance in Series

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

Enforceability of Rights by Holders of Units

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

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

Anti-Takeover Provisions of our Certificate of Incorporation and Bylaws

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

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

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

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

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

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

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

Provisions of Delaware Law Governing Business Combinations

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

- prior to such date, the board of directors approved either the "business combination" or the transaction which resulted in the "interested stockholder" obtaining such status; or

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

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

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

Limitations on Liability and Indemnification of Officers and Directors

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

LEGAL MATTERS

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

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2010, and the effectiveness of our internal control over financial reporting as of December 31, 2010, as set forth in their reports, which are incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's web site at http://www.sec.gov. Our common stock is listed on The Nasdaq Global Market, and you can read and inspect our filings at the offices of the Financial Industry Regulatory Authority at 1735 K Street, Washington, D.C. 20006.

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

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

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to "incorporate by reference" information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus, and information that we file later with the SEC will automatically update and supersede this information. We filed a registration statement on Form S-3 under the Securities Act of 1933, as amended, with the SEC with respect to the securities we may offer pursuant to this prospectus. This prospectus omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities we may offer pursuant to this prospectus. Statements in this prospectus regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the 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 fiscal year ended December 31, 2010 filed on March 11, 2011;
- our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2011 filed on May 5, 2011;
- our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2011 filed on August 4, 2011;
- our Current Reports on Form 8-K filed on January 14, 2011, February 9, 2011, March 1, 2011, April 4, 2011, April 15, 2011, April 22, 2011, June 6, 2011, June 15, 2011, June 27, 2011, July 7, 2011, and July 21, 2011;
- the portions of our Definitive Proxy Statement on Schedule 14A filed on April 29, 2011 that are deemed "filed" with the SEC under the Exchange Act;
- the description of our common stock contained in our Registration Statement on Form 8-A filed on January 26, 2007, including any amendment or report filed for the purpose of updating such description; and
- all reports and other documents subsequently filed by us pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act after the date of this prospectus and prior to the termination or completion of the offering of securities under this prospectus shall be deemed to be incorporated by reference in this prospectus and to be a part hereof from the date of filing such reports and other documents.

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

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

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

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

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3,976,702 Shares of Common Stock

PROSPECTUS SUPPLEMENT

July 25, 2012