UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2012

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission file number: 001-33277

SYNTA PHARMACEUTICALS CORP.
(Exact name of registrant as specified in its charter)

Delaware	**04-3508648**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
45 Hartwell Avenue **Lexington, Massachusetts** (Address of principal executive offices)	**02421** (Zip Code)

Registrant's telephone number, including area code **(781) 274-8200**

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.0001 Par Value Per Share	The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Exchange Act: **None.**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer," and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐	Accelerated filer ☒	Non-accelerated filer ☐ (Do not check if a smaller reporting company)	Smaller reporting company ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant (without admitting that any person whose shares are not included in such calculation is an affiliate), computed by reference to the price at which the common stock was last sold on June 30, 2012, the last business day of the registrant's most recently completed second fiscal quarter, was $206,423,923.

As of March 8, 2013 the registrant had 69,054,951 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

The following documents (or parts thereof) are incorporated by reference into the following parts of this Annual Report on Form 10-K: Certain information required in Part III of this Annual Report on Form 10-K is incorporated from the registrant's Proxy Statement for the 2013 Annual Meeting of Stockholders.

PART I

Item 1. BUSINESS

The Company

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

In 2012, we made significant progress with the development of our lead drug candidate, ganetespib, which is currently being evaluated in a broad range of trials including lung, breast, and other solid tumor and hematologic cancers. Over 20 clinical trials with ganetespib are ongoing, recently completed, or currently initiating.

Key achievements in 2012 include:

- At the European Society for Medical Oncology (ESMO) 2012 Congress in Vienna, Austria, investigators reported encouraging interim results from the first 172 patients enrolled in our 300-patient GALAXY-1 trial, a global, randomized study comparing standard-of-care docetaxel alone and in combination with ganetespib as second-line treatment of advanced non-small cell lung cancer (NSCLC) with adenocarcinoma histology.

- Completed target enrollment of the first 240 patients of GALAXY-1 and progressed to the expansion stage, enrolling an additional 60 patients with certain prespecified NSCLC disease characteristics.

- Initiated GALAXY-2, a 500-patient, global, randomized, confirmatory Phase 3 clinical trial evaluating ganetepsib plus docetaxel vs. docetaxel alone for the treatment of second-line advanced NSCLC, as with GALAXY-1. Results from the GALAXY-1 interim analysis were used to inform the design of GALAXY-2, enriching for those patients who showed enhanced clinical benefit from treatment with ganetespib.

- Initiated the CHIARA and ENCHANT company-sponsored clinical trials to evaluate ganetespib monotherapy in ALK+ NSCLC and HER-2+ or triple-negative metastatic breast cancer, respectively.

- Initiated a number of investigator-sponsored trials evaluating ganetespib with other widely used cancer drugs. Outcomes of these studies may inform future company-sponsored trials with ganetespib.

- Presented and published preclinical results demonstrating the activity of ganetespib in various preclinical models of genetically-defined cancers, as well as activity with commonly used chemotherapeutic and targeted therapies and other experimental agents.

- Presented results at the American Society of Clinical Oncology (ASCO) meeting in June 2012 showing 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.

- Established in preclinical models that ganetespib inhibits new blood vessel formation (angiogenesis) and reduces tumor spread (metastasis). Showed in preclinical models that

treatment with ganetespib leads to the destabilization and degradation of key proteins known to drive angiogenesis and metastasis.

- Demonstrated in patients that treatment with ganetespib inhibits certain key cancer-promoting proteins, such as hypoxia induced factor 1 alpha (HIF-1alpha) and vascular endothelial growth factor (VEGF), believed to contribute to both angiogenesis and growth of metastases.

In addition to progress with our ganetespib program, we also made significant progress with our elesclomol and calcium release activated channel M1 (CRACM) inhibitor programs. We continued development of elesclomol in patients with advanced ovarian cancer, a trial being conducted by the Gynecologic Oncology Group (GOG) and supported by the National Cancer Institute (NCI), and in patients with acute myeloid leukemia (AML). The ovarian cancer trial has met the pre-specified response rate efficacy requirement to advance to stage 2 and full enrollment. Evaluation of several of our CRACM inhibitor compounds showed favorable safety and activity in animal models of inflammatory disease.

We believe that the broad clinical and commercial potential of our drug candidates, together with our operational capabilities and additional competitive advantages, provide us with multiple, sustainable growth opportunities. Our capabilities and advantages include: our intellectual property portfolio, consisting of over 800 issued and pending patents; the full ownership of all commercial rights in all geographic regions to our programs; our ability to integrate discovery, translational, and clinical research to optimize our development programs and further strengthen our intellectual property position; our operational experience in effectively managing large-scale, global clinical programs; our strong network of relationships with leading investigators and medical centers; our proprietary chemical compound library and the strength of our drug discovery platform; and the skills, talent, and level of industry experience of our employees.

Company Strategy

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

- exploiting the unique, first-in-class / best-in-class potential of our existing drug candidates to establish and achieve sustainable advantages relative to other therapeutic options;

- using our translational research and biomarker identification capabilities, together with our collaborations with leading researchers and investigators, to identify the patient populations most likely to derive benefit from our drug candidates and using those findings to optimize our clinical trial choices;

- maintaining the flexibility to partner or retain individual programs, globally or regionally, to achieve creative and favorable partnership structures;

- maintaining a strong cash position, such that we have multiple options for continuing to advance our drug candidates either on our own or with a partner;

- using our discovery and development capabilities to expand and protect our intellectual property position for each of our programs; and

- using our proprietary compound library and discovery platform to continue to generate promising new drug candidates with distinct chemical structures, novel mechanisms of action, and broad therapeutic potential.

Our Drug Candidate Pipeline

The following table summarizes the current status of our most advanced research and development programs:

	Product Candidate	Trial	Stage	Development Status
Oncology	**Ganetespib** Hsp90 inhibitor *(Key ongoing / initiating company-sponsored trials)*	Adenocarcinoma NSCLC, second-line, randomized, docetaxel +/- ganetespib (GALAXY-2)	Phase 3	Initiating
		Adenocarcinoma NSCLC, second-line, randomized, docetaxel +/- ganetespib (GALAXY-1)	Phase 2b/3	Enrolled last patient of 240-patient initial target in November 2012; overall survival analysis 6-months from last patient expected Q2 2013; final PFS and 12-month OS results expected 2H 2013
		ALK+ NSCLC (CHIARA)	Phase 2	Ongoing
		Breast cancer (ENCHANT)	Phase 2	Ongoing
		NSCLC, monotherapy	Phase 2	Completed
	(Key ongoing / initiating third-party sponsored trials)			
		Breast cancer, combination with Herceptin, Taxol	Phase 2	Initiating
		Mesothelioma, combination with pemetrexed, cisplatin	Phase 1/2	Initiating
		HR+ breast cancer, combination with fulvestrant	Phase 2	Ongoing
		ALK+ lung cancer, combination with crizotinib	Phase 1/2	Ongoing
		Acute myeloid leukemia, combination with ara-C	Phase 2	Ongoing
		Rectal cancer, combination with radiotherapy	Phase 2	Ongoing
		Multiple myeloma, combination with Velcade	Phase 1/2	Ongoing
	Additional Hsp90 inhibitors	Cancer	Preclinical development	Ongoing
	Elesclomol Mitochondria-targeting agent	Ovarian cancer	Phase 2	Ongoing
		Acute myeloid leukemia	Phase 1	Ongoing
	STA-9584 Vascular disrupting agent	Prostate cancer	Preclinical development	Ongoing
Inflammatory Diseases	**CRACM channel inhibitors**	Autoimmune diseases Respiratory conditions Transplant	Preclinical development	Ongoing

IL-12/23 inhibitors	Autoimmune diseases	Lead optimization	Ongoing

We retain full ownership of all of our drug candidates.

In the above table and throughout this report, lead optimization indicates a stage at which compounds have shown activity, selectivity, and efficacy in animal models, as well as an acceptable preliminary safety profile. These compounds are being optimized for selectivity and potency, drug-like properties, and safety before entering into preclinical development. Preclinical development activities include manufacturing, formulation, pharmacology and toxicology studies prior to initiating a Phase 1 clinical trial. Phase 1 indicates initial clinical safety testing and pharmacological profiling in healthy volunteers, with the exception that Phase 1 clinical trials in oncology are typically performed in patients with cancer. Phase 2 involves efficacy testing and continued safety testing in patients with a specific disease. There are multiple types of Phase 2 trials: Phase 2 trials may include a Phase 1 dose-escalation stage (Phase 1/2); they may be single-arm, with relatively few patients (Phase 2a); or they may be randomized and controlled, with a larger number of patients (Phase 2b). Phase 3 indicates a confirmatory study of efficacy and safety in a larger patient population, and may involve comparison with placebo, standard treatments, or other active comparators.

Oncology Programs

We have two clinical-stage programs and several preclinical-stage programs in oncology. Our clinical-stage drug candidates include:

- *Ganetespib, Hsp90 inhibitor:* Ganetespib is a potent, synthetic, small molecule inhibitor of heat shock protein 90 (Hsp90), a chaperone protein that is essential to the function of certain other proteins, such as tyrosine kinases and transcription factors that drive the growth, proliferation, and survival of many different types of cancer. Ganetespib is currently being evaluated in a broad range of clinical trials both in combination with other therapies and as a single agent. In 2011, we initiated the GALAXY-1 clinical trial, a 300-patient, global, randomized, Phase 2b/3 study of ganetespib in combination with docetaxel vs. docetaxel alone in patients with advanced NSCLC who had progressed following one prior treatment for advanced disease (second-line patients). In the fourth quarter of 2012, we initiated GALAXY-2, a 500-patient, global, randomized, confirmatory Phase 3 clinical trial evaluating ganetespib plus docetaxel vs. docetaxel alone in second-line advanced NSCLC, as with GALAXY-1. Results from an interim analysis of the GALAXY-1 trial conducted in September 2012 were used to inform the design of GALAXY-2, enriching for those patients who showed enhanced clinical benefit from treatment with ganetespib in GALAXY-1. In mid-2012, we also initiated the CHIARA trial, a Phase 2 single-arm study evaluating ganetespib monotherapy as treatment for ALK+ NSCLC patients naïve to ALK inhibitor therapy, as well as the ENCHANT trial, a Phase 2 study evaluating ganetespib monotherapy as front-line treatment of HER2+ or triple negative metastatic breast cancer. In 2013, in addition to company sponsored trials, we are planning initiation of several ganetespib trials which are sponsored by third parties, including individual investigators and cooperative groups.

- *Elesclomol, mitochondria-targeting agent.* Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death (apoptosis) in cancer cells by disrupting cancer cell mitochondrial metabolism. Elesclomol is currently in a clinical trial in ovarian cancer in combination with paclitaxel and a clinical trial in AML as a single agent. In a preplanned interim analysis, the ovarian cancer trial has met the prespecified efficacy requirement to advance to stage 2 and full enrollment.

Oncology Background

Cancers are diseases characterized by abnormal and uncontrolled cell growth and division, which typically leads to tumor formation. Growing tumors can directly disrupt organ function at sites of

origin, and can also spread by a process known as metastasis to other organs, such as the brain, bones and liver. The growth of metastatic tumors at these new sites can disrupt the function of other organs. There are many kinds of cancer, but all are characterized by uncontrolled growth of abnormal cells.

The World Health Organization estimates that more than 12 million people are diagnosed with cancer every year worldwide, and approximately 8 million people die from the disease annually. The American Cancer Society estimates that approximately 1.7 million people in the United States will be diagnosed with cancer in 2013, and approximately 580,000 people will die from the disease.

According to IMS Health, oncology products are the largest therapeutic class of pharmaceuticals in the world with global sales of $56.0 billion in 2010.

Ganetespib (Hsp90 Inhibitor)

Summary

Ganetespib is a novel, potent, small molecule inhibitor of 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 these 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 anti-cancer agents may provide greater benefit than those agents administered alone. In preclinical studies, ganetespib has shown potent anti-cancer activity against a broad range of solid and hematologic cancers, both as a monotherapy and in combination with certain widely used anti-cancer agents.

Ganetespib is currently being evaluated in a broad range of cancer clinical trials including our 800-patient GALAXY NSCLC program (GALAXY-1 and GALAXY-2) in combination with docetaxel chemotherapy, and as monotherapy in certain genetically-defined targeted patient populations. A favorable safety profile has been consistently observed across clinical trials, involving over 700 patients treated with ganetespib to date. 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 the clinical trials conducted to date, ganetespib has shown promising activity in a broad range of cancers, both in combination with chemotherapy and as a monotherapy.

- *Combination:* At the ESMO 2012 Congress, investigators presented encouraging results from the second interim efficacy analysis of GALAXY-1, including the following:

    - In the 172 NSCLC patients with adenocarcinoma histology evaluated as of the September 10, 2012 data cutoff date, an increase in overall survival was observed in patients treated with ganetespib plus docetaxel versus patients receiving docetaxel alone. A median overall survival of 7.4 months was observed in the docetaxel control arm, while median overall survival had not yet been reached in the ganetespib arm. Overall survival results for the docetaxel arm were consistent with historical results from prior second line NSCLC therapy trials.

    - Objective response rate and progression-free survival in adenocarcinoma patients were also improved from 8% to 16%, and from 2.8 months to 4.2 months, in the control arm vs. ganetespib arm, respectively. Overall response and progression-free survival rates in the control arm were consistent with results from prior trials with docetaxel in this setting.

- Results in several GALAXY patient subpopulations, defined by pre-specified clinical and biomarker characteristics, showed a substantially improved survival difference between the control arm and ganetespib arm, as compared with the difference in the all-comer (intent-to-treat or ITT) adenocarcinoma patient population. These findings have been incorporated into the design of the confirmatory Phase 3 GALAXY-2 trial to enrich for patients most likely to derive the greatest benefit from ganetespib treatment.

- Clinical and preclinical results were presented that suggest ganetespib treatment has anti-angiogenic and anti-metastatic effects. Analyses of tumor samples from rectal cancer patients treated with ganetespib showed a reduction of levels of HIF-1alpha and VEGF. In addition, preclinical experiments demonstrated strong inhibition of tumor vasculature by ganetespib. These results suggest ganetespib offers a novel way to inhibit angiogenesis and tumor spread (metastasis): by reducing production of multiple angiogenesis and metastasis-promoting factors simultaneously, rather than targeting specific signaling factors directly with antibodies or kinase inhibitors.

- A favorable safety profile was observed with the ganetespib plus docetaxel combination in adenocarcinoma patients. Transient, mild-to-moderate diarrhea was the most common adverse event, consistent with observations from other clinical trials evaluating ganetespib. Other adverse events increased relative to control included mild to moderate anemia and fatigue, as well as a small increase in the number of cases of febrile neutropenia.

- *Monotherapy:*

- Objective responses or anti-tumor activity have been seen in patients with ALK+ NSCLC, mutant BRAF lung cancer, mutant KRAS NSCLC cancer, mutant KRAS gastric cancer, HER2+ breast cancer, HER2+ gastric cancer, triple-negative breast cancer, renal cancer, colorectal cancer, and melanoma. One patient with ALK+ NSCLC cancer and one patient with mutant KRAS gastric cancer have durable responses and have remained on ganetespib therapy for over two years.

The results observed to date in our GALAXY program suggest a significant commercial opportunity for use of ganetespib in combination with docetaxel as second-line treatment of NSCLC adenocarcinoma. Across the United States, United Kingdom, Germany, France, Spain, Italy, and Japan an estimated 160,000 new patients each year progress following first-line treatment for advanced NSCLC adenocarcinoma and receive subsequent treatment, which represents the patient population being addressed in our GALAXY program. In addition, over 500,000 patients receive taxanes each year (docetaxel or paclitaxel), across all cancer indications. The potential to combine ganetespib with taxanes with minimal additional toxicity and possible enhanced efficacy represents a promising opportunity not only in lung cancer but in breast, prostate, ovarian, gastric, bladder, and head and neck cancers, where taxanes are commonly used. 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.

In the fourth quarter of 2012, we initiated the Phase 3 GALAXY-2 trial, which compares the same treatment regimen of ganetespib plus docetaxel in combination vs. docetaxel alone, at the same dose and schedule, in the same cancer indication as was evaluated in the GALAXY-1 trial. GALAXY-2 will enroll a subpopulation of NSCLC adenocarcinoma patients that showed an enhanced benefit from the ganetespib combination therapy in GALAXY-1.

Ganetespib Mechanism of Action

Hsp90 is required for the structural and functional maturation of numerous client proteins, many of which play critical roles in cell growth, differentiation and survival. Preclinical and clinical results have shown that ganetespib is a potent and selective inhibitor of Hsp90, supporting the promise for therapeutic intervention of Hsp90 function in a broad range of malignancies. As with other physiological processes that may be redirected by tumor cells, it is has become clear that the chaperone function of Hsp90 is often subverted to facilitate growth and spread of a malignant tumor. Many research groups have shown that cancer cells exploit the Hsp90 machinery to protect a variety of mutated and/or overexpressed oncoproteins from targeted degradation. Relative to their normal counterparts, cancer cells are more reliant on elevated levels of the active Hsp90 complex and as such, appear to be selectively sensitive to Hsp90 inhibitors, including ganetespib.

A unique characteristic of targeting Hsp90 in cancer cells is that inhibition of this singular protein results in the simultaneous disruption of numerous oncogenic signaling pathways that are critical for tumor cell proliferation and survival. In addition, inhibiting Hsp90 activity has profound effects on cell cycle dynamics and DNA repair processes, since many cell cycle regulators and DNA repair components are themselves Hsp90 client proteins. Because of this impact on multiple cascades, we and others have hypothesized that inhibiting Hsp90 can bypass signaling redundancies, overcome resistance mechanisms and sensitize cancer cells to chemotherapeutic agents.

A number of sensitive Hsp90 client proteins, such as ALK, HER2, AR, mutant BRAF and EGFR, have been implicated as oncogenic drivers in a variety of human tumors, including lung, breast, prostate and melanoma. Moreover, many client proteins are the targets of marketed cancer drugs such as Avastin, Erbitux, Gleevec, Herceptin, Nexavar, Sutent, Tarceva, Votrient, Xalkori, and Zelboraf.These agents are monoclonal antibodies or kinase inhibitors that bind directly to individual protein targets to inhibit their activity. In contrast, ganetespib, through inhibition of Hsp90, simultaneously decreases the expression of many of these same targets. In preclinical studies, ganetespib has demonstrated potent single-agent activity in cancer cells that are highly dependent on these targets, including mutated and re-arranged forms that are resistant to treatment with monoclonal antibodies or kinase inhibitors. Importantly the observed *in vitro* activity has translated to robust antitumor efficacy and survival benefit *in vivo,* as we have seen in mouse models of these cancers.

Ganetespib's activity profile appears to be superior to other Hsp90 inhibitors based on the efficacy and safety data we have compiled to date. Ganetespib is a novel small molecule that is 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. Results published in *Molecular Cancer Therapeutics* in December 2011 highlighted certain physicochemical properties of ganetespib we believe contribute to its improved safety and activity relative to other Hsp90 inhibitors. These properties include smaller size, greater potency in inhibiting Hsp90, improved ability to passively enter cells, absence of a molecular component believed to cause liver toxicity, and the ability to penetrate deep into tumor tissues.

In the clinic, we believe that ganetespib has demonstrated meaningful activity as a monotherapy in ALK+ and mutant BRAF NSCLC as well as HER2+ metastatic breast and gastric cancers. Ganetespib has also shown activity in triple negative breast cancer (TNBC), suggesting that an unidentified Hsp90 client(s) down-regulated by ganetespib is likely driving progression of this disease.

Because of the broad spectrum of biological activity conferred by ganetespib treatment, an additional approach has been to combine this agent with standard of care chemotherapeutics or other molecularly-targeted agents. In this regard, we have demonstrated a clear capacity of ganetespib to augment the cytotoxic activity of DNA damaging chemotherapeutics in multiple models. In addition, our data suggest that many relevant client proteins affected by ganetespib within this context are

implicated in other critical tumorigenic processes, such as metastasis and angiogenesis. Prior work has established that regulators of tumor metastasis, such as the transcription factor HIF-1alpha, and regulators of angiogenesis, including VEGF and related receptors, are all down-regulated by ganetespib.

HIF-1alpha is a transcription factor that regulates genes involved in the growth and spread of tumors including metastasis, angiogenesis, suppression of the immune response, survival of stem or tumor-initiating cells, as well as resistance to chemotherapy, radiotherapy, and immunotherapy. HIF-1alpha is an established Hsp90 client and, in collaboration with others, we have shown the ganetespib treatment results in robust reductions of HIF-1alpha levels in cancer cells. Reduced VEGF expression, likely as a consequence of lowered HIF-1alpha activity, was also seen such that ganetespib disrupted blood vessels surrounding tumors comparable to traditional anti-angiogenic agents. Moreover, these findings were supported by data obtained by our collaborators at Emory University, who showed that tumor samples from rectal cancer patients expressed significantly lower levels of HIF-1alpha and VEGF following ganetespib treatment.

Importantly, preclinical results supporting the effects that ganetespib has on tumor biology also appear to correlate with clinical observations in our GALAXY-1 trial. Of the 39 and 26 patients that had experienced radiologic progression in both arms of the study at the time of the September 2012 GALAXY-1 analysis, 24 (62%) of the docetaxel arm and 8 (31%) of the ganetespib plus docetaxel combination arm had progressed due solely to the formation of new lesions. These results suggest that the survival improvement observed in patients treated with ganetespib may be linked to the ability of the drug candidate to inhibit or reduce the growth of metastatic lesions, the primary contributor of cancer patient mortality.

Ganetespib Clinical Trials

We are sponsoring four principal ongoing trials evaluating ganetespib activity:

- GALAXY-1: a 300-patient global, randomized Phase 2b/3 trial designed to evaluate ganetespib in combination with docetaxel versus docetaxel alone as second-line therapy in advanced NSCLC patients with adenocarcinoma histology

- GALAXY-2: a 500-patient, global, randomized, confirmatory Phase 3 clinical trial evaluating ganetespib plus docetaxel vs. docetaxel alone for the treatment of second-line advanced NSCLC, as with GALAXY-1. Results from an interim analysis of the GALAXY-1 trial conducted in September 2012 were used to inform the design of GALAXY-2, enriching for those patients who showed enhanced clinical benefit from treatment with ganetespib in GALAXY-1;

- CHIARA: a Phase 2 trial evaluating ganetespib monotherapy in NSCLC patients whose tumors have a genetic profile characterized by rearrangement of the ALK gene (ALK+); and

- ENCHANT: a Phase 2 trial evaluating ganetespib monotherapy in patients with newly diagnosed HER2+ and triple-negative metastatic breast cancer.

The GALAXY program: ganetespib in lung cancer

Cancer treatments are often given in combination with one another in order to maximize likelihood of treatment benefit. A challenge with combination therapy, however, is that the added toxicities are often intolerable particularly if toxicity profiles overlap. The favorable safety profile seen in studies to date with ganetespib and the non-overlapping toxicities with many standard-of-care cancer therapies support such a combination therapy approach with this drug candidate. Specifically, we believe that there is particular potential for combining ganetespib and taxanes, such as docetaxel and paclitaxel. Supporting evidence include a strong scientific rationale based on multiple mechanisms of synergistic anti-cancer activity, strong synergistic results in *in vitro* and *in vivo* experiments, and the

encouraging safety profiles seen in our Phase 1 and GALAXY-1 studies combining ganetespib and docetaxel.

GALAXY Program Design

In 2011 we initiated the GALAXY-1 trial in patients with advanced NSCLC who received one prior treatment for advanced disease, i.e., a second-line treatment setting. GALAXY-1 compares treatment with docetaxel alone, which is approved for second-line treatment, versus treatment with ganetespib plus docetaxel. The aim of this study is to 1) evaluate clinical benefit and establish the safety profile of ganetespib in combination with docetaxel relative to docetaxel alone, 2) identify the patient populations, by biomarker or other disease characteristics, which may be most responsive to combination treatment, and 3) to build the clinical and operational experience needed to optimize the design and execution of a pivotal Phase 3 registration trial.

Patients in both arms of GALAXY-1 receive a standard regimen of docetaxel 75 mg/m2 on day 1 of a 21-day treatment cycle. Patients in the combination arm also receive ganetespib 150 mg/m2 on days 1 and 15. Treatment continues until disease progression or until patients become intolerant. Treatment groups are stratified by ECOG performance status, lactate dehydrogenase (LDH) levels, smoking status, and time since diagnosis of metastatic disease to ensure balance of these prognostic factors between the two arms.

GALAXY-1 was originally designed to enroll 240 second-line advanced NSCLC patients in order to evaluate several pre-specified hypotheses on which patients might be most responsive to combination treatment. Co-primary endpoints were progression-free survival in all patients (the ITT 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.

GALAXY-1 was also originally designed to enroll patients with all histologies—including adenocarcinoma, squamous cell carcinoma, large cell carcinoma and other histologies. In early 2012, enrollment of patients with non-adenocarcinoma histologies (which consists primarily of squamous cell carcinomas) was terminated based on possible safety concerns, including risk of bleeding; a trend towards inferior survival; and the consistency of the emerging ganetespib profile with known anti-angiogenic agents, for which patients with squamous cell carcinoma histology are commonly excluded from clinical trials or labeled indications. The trial was amended at that time to enroll 240 patients with adenocarcinoma histology only.

The current co-primary endpoints of GALAXY-1 are PFS in patients with elevated LDH and PFS in patients with mutant KRAS. Both of these represent patient populations with high unmet medical needs and for which there are encouraging preclinical and early clinical results supporting the use of ganetespib. Key secondary endpoints, which have been evaluated with the statistical gatekeeping methodology, include OS and PFS in the all-adenocarcinoma population. GALAXY-1 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 overall survival from 6 to 8.5 months. All powering assumptions are based on a 1-sided alpha of 0.05.

GALAXY-1 Interim Results

In June 2012, we reported top line results from a planned interim analysis of GALAXY-1. The analysis was planned for when approximately 50% of patients had been enrolled. At the time of this analysis, a total of 114 adenocarcinoma and 69 non-adenocarcinoma patients had been enrolled.

On September 29, 2012, we reported results from the second interim efficacy analysis at the European Society for Medical Oncology (ESMO) 2012 Congress. This analysis was planned for when approximately 80% of patients had been enrolled. At the time of the September 10, 2012 data cutoff date, 187 adenocarcinoma patients had been enrolled in the trial and results from 172 patients were entered into the clinical database, with 88 patients in the docetaxel arm and 84 patients in the ganetespib arm. Baseline characteristics were generally well balanced between both arms. An additional analysis was planned for patients who would have a minimum of 6 months of follow-up, defined by those patients enrolled before March 20, 2012. There were 38 patients in the docetaxel control arm and 39 patients in the ganetespib arm in this group. Baseline characteristics were also generally well balanced between both arms in this group. Overall survival results are described in the table below. Median survival for the docetaxel control arm in both the ITT and the 6-month follow up groups was consistent with comparable historical results. Median survival had not yet been reached for the combination arm.

Overall survival, all adenocarcinoma patients

	All patients in database (N=172)	All patients enrolled more than 6 months prior to data cutoff (N=77)
HR	0.688	0.568
C.I. (90%)	(0.417, 1.135)	(0.312, 1.032)
p-Value	0.183	0.056
Median (D vs G+D)	7.4 mo vs. NR	7.4 mo vs NR

HR: Hazard ratio, C.I.: confidence interval, NR: not reached

Hazard ratio (HR) represents the odds that a patient in the experimental treatment arm will experience the event of interest (such as death or disease progression) before a patient in the control arm. A hazard ratio of 1.0 corresponds to no treatment effect, while a hazard ratio of less than 1.0 signifies that the treatment is working better than the control.

Progression free survival was 2.8 months vs. 4.2 months (p=0.076) and overall response rate was 8% vs. 16% (p=0.078) for docetaxel vs. ganetespib plus docetaxel, respectively. All p-values are calculated using the 1-sided stratified log-rank test for survival endpoints and using Fisher's Exact test for response rate.

GALAXY-1 design has four pre-specified stratification factors and one additional biomarker defined primary endpoint subpopulation (mKRAS patients). Results for these patient populations are shown below.

Overall survival, pre-specified subpopulations and stratification groups

LDH	Elevated	Normal
N	49	123
HR	0.67	0.69
C.I. (90%)	(0.33,1.37)	(0.33,1.40)
p-Value	0.18	0.19

KRAS	Mutant	Wild-type/ND
N	38	94
HR	0.41	0.72
C.I. (90%)	(0.15,1.16)	(0.36,1.45)
p-Value	0.07	0.22

Time since diagnosis of advanced Disease	>6 mo	<=6 mo
N	108	51
HR	0.37	1.83
C.I. (90%)	(0.18,0.77)	(0.80,4.19)
p-Value	0.01	0.89

Smoking status	Never/past	Current
N	130	42
HR	0.48	1.61
C.I. (90%)	(0.26,0.90)	(0.67,3.89)
p-Value	0.02	0.81

ECOG Performance Status	0	1
N	80	92
HR	0.75	0.72
C.I. (90%)	(0.33,1.73)	(0.38,1.35)
p-Value	0.29	0.19

ND: not determined

Results in several of these patient subpopulations showed a substantially improved survival difference between the control arm and ganetespib arm, as reflected in a substantially lower hazard ratio as compared with the all-comers, or intent-to-treat (ITT), patient population. In the population of patients whose diagnosis of advanced disease was greater than six months prior to study entry (N=108), a hazard ratio of 0.37 (90% C.I. 0.18-0.77, p=0.01) was observed, supporting the potential for enhanced activity of ganetespib in this subpopulation. At the time of the September 10, 2012 analysis, only 159 of the 172 total patients had their date of study entry entered into the clinical database. Completing the data collection yielded an additional nine patients meeting the criterion of diagnosis of advanced disease greater than six months prior to study entry. The results for the hazard ratio, or benefit from treatment with ganetespib, in this larger 117-patient group were comparable to the 108-person group presented at ESMO: the hazard ratio was 0.33 (90% C.I. 0.17-0.75, p=0.01).

The adverse event profile of GALAXY-1 was comparable between both arms. The proportion of adenocarcinoma patients with at least one adverse event (AE) was 69% vs. 90%; with grade 3 or 4 AEs was 37% vs. 56%; with AEs leading to treatment discontinuation was 8% vs. 15%; and with AEs with outcome of death were 8% vs. 7%, for D (N=86) vs. G+D (N=81), respectively. The most common AEs, all grades were neutropenia (50% vs. 49%), diarrhea (12% vs. 42%) and fatigue (20% vs. 31%), for D vs. G+D, respectively. Diarrhea and fatigue were predominantly grade 1 and grade 2; the incidence of grade 3 or 4 diarrhea was 0% vs. 4% and grade 3 or 4 fatigue was 2% vs. 5% in D vs. G+D, respectively. The most common grade 3 or 4 AEs were neutropenia (34% vs. 35%), febrile neutropenia (2% vs. 10%), and fatigue (2% vs. 5%). Compared to other Hsp90 inhibitors, there were relatively few reported incidences of ocular toxicity, 4 (5%) in the G+D arm and 1 (1%) in the D arm, all of which were transient and grade 1 or 2. None of the ocular toxicity cases were described as visual impairment.

Enrollment in GALAXY-1

In October 2012, GALAXY-1 achieved its targeted enrollment of 240 adenocarcinoma patients. Twelve additional patients were in screening at the time target enrollment was met, yielding a total of 252 adenocarcinoma patients randomized. Overall survival analyses planned for 6 months and 12 months after the last patient enrolled in this population are expected to be conducted in the second quarter and fourth quarter of 2013, respectively.

The GALAXY-1 protocol specifies that following completion of the target number of adenocarcinoma patients, enrollment of patients in two pre-specified subpopulations may continue in order to ensure a sufficient number of patients in each of those subpopulations. We expect that approximately 60 additional patients will be enrolled, in order to achieve a cumulative total of approximately 120 patients with elevated LDH and 80 patients with mutant KRAS. We expect that that the final PFS analyses for these GALAXY-1 subpopulations will be conducted in the second half of 2013.

Initiation of GALAXY-2

In November 2012, we participated in an End-of-Phase 2 (EOP2) meeting with the U.S. Food and Drug Administration (FDA) to review plans for the 500-patient, global, randomized Phase 3 GALAXY-2 clinical trial. We have incorporated comments from this meeting into the protocol, and expect enrollment to begin in the first quarter of 2013.

The GALAXY-2 trial will enroll adenocarcinoma patients with advanced NSCLC who have received one prior treatment for metastatic disease, and will randomize those patients 1:1 to treatment with docetaxel plus ganetespib, or docetaxel alone, as with GALAXY-1.

The same dose and schedule used in GALAXY-1 will be used in the Phase 3 GALAXY-2 trial. Patients on both arms will receive docetaxel generally for four to six 21-day cycles, according to standard practice at their treatment center. After completion of docetaxel treatment, patients on the ganetespib arm are eligible to continue to receive ganetespib monotherapy as maintenance treatment. The trial will be conducted in many of the 60 centers across Europe and North America that participated in the GALAXY-1 trial, together with approximately 60 additional centers.

Results from the interim analysis for GALAXY-1 were used to inform the eligibility criteria for the GALAXY-2 trial. GALAXY-2 will enroll patients who have progressed following treatment with one prior platinum-containing regimen of chemotherapy as first-line therapy, and who were diagnosed with metastatic disease at least six months prior to study entry.

The primary endpoint of GALAXY-2 will be overall survival. Two event-driven interim analyses of the overall survival primary endpoint of GALAXY-2 have been specified. Based on current projections and statistical assumptions, we expect these analyses, together with the final overall survival analysis, to occur in 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 profile.

Encouraging evidence of clinical activity was also observed in this trial, as evidenced by the durable objective tumor responses achieved in certain patients. 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 >24 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 anti-cancer agents in these advanced NSCLC treatment settings, for which objective response rates have been in the range of 5-10%.

To further characterize ganetespib activity in this treatment setting, we initiated the CHIARA trial in 2012 to evaluate ganetespib monotherapy in ALK+ NSCLC patients who have not been previously treated with a direct ALK inhibitor. We expect to use results from an initial phase of enrollment, which was completed in the first quarter of 2013, to inform our decision on whether to continue additional enrollment in this trial.

Preclinical results from experiments conducted in our laboratories have demonstrated synergy between ganetespib and crizotinib as well as other direct ALK inhibitors. These data support the potential for treating ALK+ NSCLC patients with a combination of ganetespib and direct ALK inhibitors. An investigator-sponsored Phase 1/2 trial evaluating ganetespib in combination with crizotinib in patients with ALK+ NSCLC that have not been previously treated with an ALK inhibitor began enrolling patients at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City in 2012.

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 cancer 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.

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 may show activity in TNBC.

In 2012, we initiated the ENCHANT trial designed to evaluate ganetespib monotherapy as first-line treatment for both metastatic HER2+ breast cancer and TNBC. Patients in both cohorts will be assessed at baseline and at weeks 3, 6, and 12 with a combination of PET and CT scans. The primary endpoint of this study is overall response rate at week 12. Up to 35 patients will be enrolled in each of the HER2+ and TNBC cohorts.

In addition to evaluating monotherapy administration of ganetespib in breast cancer, we and our collaborators believe that combination therapy with ganetespib has promise. 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 2013, a number of ganetespib trials sponsored by third parties, including cooperative groups, foundations, and individual investigators, have recently been initiated or are expected to initiate in 2013, including:

- 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 in 2012;
- 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 in 2012;
- a trial evaluating both ganetespib monotherapy and the combination of ganetespib and bortezomib in multiple myeloma, which began enrolling patients in 2012, and is supported by a grant of up to $1 million by the Multiple Myeloma Research Foundation;
- a randomized trial evaluating the combination of ganetespib and low dose ara-C chemotherapy in elderly patients with acute myeloid leukemia (AML) being conducted at Cardiff University, which began enrolling patients in 2012; and
- a trial evaluating ganetespib in combination with pemetrexed and cisplatin in patients with malignant pleural mesothelioma, being sponsored by Cancer Research UK, which we expect to begin enrolling patients in the first half of 2013.

In addition, a European cooperative group plans to initiate a randomized trial comparing paclitaxel with and without ganetespib in patients with advanced ovarian cancer in 2013.

Elesclomol (Mitochondria-Targeting Agent)

Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death (apoptosis), in cancer cells through a novel mechanism: disrupting cancer cell mitochondrial metabolism. In preclinical experiments, anti-cancer activity of elesclomol has been shown to correlate with certain biomarkers, including LDH, which can distinguish between active mitochondria (sufficient oxygen present) and inactive mitochondria (insufficient oxygen present). 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 acute myeloid leukemia (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 upper limit of normal (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. The ovarian cancer trial has met the prespecified efficacy requirement to advance to stage 2 and full enrollment of the Phase 2 study, indicating potential activity in this difficult-to -treat patient population with limited treatment options.

STA-9584 (Vascular Disrupting Agent)

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

Our Inflammatory Disease Programs

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

CRACM Ion Channel Inhibitors

We have developed novel, small molecule inhibitors of CRACM ion channels expressed on immune cells. Our CRACM ion channel inhibitors have shown 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 Hoffman-La Roche, or 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.

On November 16, 2011, we received notice from Roche of its election to terminate the Roche Agreement, which termination became effective on February 16, 2012. Roche's termination of the agreement falls under the "Termination for Convenience" clause of the agreement. 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

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

Our Drug Discovery Capabilities

Our drug discovery approach is based on the close integration and rapid cycle times among our chemistry, biology, and pharmaceutical development groups. Drug candidates are typically identified using novel chemical structures from our chemical compound library in cell-based assays that are designed to preserve the complexity of biological signaling. Early *in vivo* testing and a rapid optimization process allow us to generate a high number of promising leads from our screening hits, improve the profiles of our compounds, and, in some cases, discover novel pathways or mechanisms of action with the potential to define entirely new categories of treatment.

Our approach integrates the following capabilities and resources:

- *Unique chemical compound library.* Our chemical library contains over 100,000 small molecules and numerous plant extracts collected from universities, non-profit institutions, other organizations, and commercial sources. Many of our compounds are proprietary and not available from commercial sources. This library represents a diverse and distinct set of chemical structures that was not generated using combinatorial chemistry and continues to be a valuable source of lead compounds for drug discovery. We are continuing our compound collection efforts. In addition, for each of our discovery programs we build focused libraries dedicated to particular drug targets. We have modeled the three-dimensional structure of most of our compounds, allowing us to use computer-based, or *in silico*, screening to identify new drug candidates.

- *Broad set of screening assays.* We have high throughput screening capabilities linked to our chemical library that facilitate the rapid identification of new drug candidates. We have developed a wide variety of biochemical and cell-based *in vitro* assays designed to identify promising compounds for treating cancer, immune disorders and other diseases, which form the basis of our initial screening efforts. In addition to assays for identifying new compounds, we have also developed assays we use for early optimization of safety and pharmacokinetic properties.

- *Robust in vivo testing capabilities.* We have substantial *in vivo* testing facilities that we use for evaluating the safety, efficacy, and pharmaceutical properties of our compounds, including absorption, distribution, metabolism, elimination, and toxicology properties. These facilities are equipped for detailed experimental measurements and surgical tasks, such as the rodent microsurgery we use for sophisticated toxicology assessments. We have experience with a wide range of animal models of disease, including multiple models in cancer, inflammatory diseases and metabolic diseases. We believe the ability to complete early testing of compounds *in vivo*,

internally and without dependence on third parties, is a valuable advantage in our ability to rapidly optimize the pharmaceutical properties of our most promising compounds.

- *Multi-functional chemistry capabilities.* We possess a full range of chemistry capabilities, including medicinal chemistry, analytical chemistry, physical chemistry, process development and computational chemistry. Our approach to medicinal chemistry applies the rigorous exploration of permutations of biologically active molecular components to optimize lead compounds. Our in-house process development capability of characterizing and specifying manufacturing processes for our compounds allows us to reduce dependence on third parties and is an important advantage in our ability to successfully commercialize our drug candidates.

- *Methods for novel target elucidation and validation.* Our scientists use expression profiling, RNA interference, affinity purification, proteomics, electrophysiology, and other methods to identify the therapeutic intervention points of novel, promising compounds.

Manufacturing

Our drug candidates and preclinical compounds are small molecules that can be readily synthesized by processes that we have developed. Utilizing our medicinal chemistry and process development capabilities, we have developed manufacturing processes to produce the active pharmaceutical ingredient (API), for our drug candidates. We also have the internal capability to synthesize small molecule compounds in quantities sufficient for use in our preclinical studies, including proof-of-concept studies in animal models, early pharmacokinetic assays, initial toxicology studies, and formulation development. We currently contract with third parties for the synthesis of all API and drug product (DP) materials used in our clinical trials and rely on third-party manufacturers for the supply of our drug candidates in bulk quantities and for the production of suitable dosage forms.

The starting materials and reagents required for synthesizing our drug candidates and preclinical compounds are commercially available from multiple sources. We have established a quality control and quality assurance program, including a set of standard operating procedures, analytical methods, and specifications, designed to ensure that our drug candidates are manufactured in accordance with the FDA's current Good Manufacturing Practice regulations (cGMPs), and other applicable domestic and foreign regulations. We have selected manufacturers that we believe comply with cGMP and other applicable regulatory standards. We do not currently expect to manufacture cGMP material internally for our clinical trials nor undertake the commercial scale manufacture of our drug candidates after approval. We are currently discussing with our current suppliers and other third-party manufacturers the long-term supply and manufacture of these and other drug candidates we may develop.

Ganetespib Manufacturing

We believe that the manufacturing processes for ganetespib API and DP are conventional and fully scalable. We also believe that the various steps of these processes can be accomplished by many possible third-party contract manufacturing organizations (CMOs). We currently use a single CMO in the preparation of the ganetespib API but we have a backup CMO that has previously manufactured ganetespib API on our behalf. We currently use a single CMO for manufacturing ganetespib DP that has specific experience in manufacturing oncology products and has flexible scale manufacturing capabilities. We have screened other CMOs for potential back up if needed in the future, and we believe that the manufacturing process for ganetespib DP can be effectively transferred to one of the already screened CMOs. We believe that the agreements we have entered into to date with these CMOs are sufficient for our current requirements.

Elesclomol Manufacturing

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

Sales and Marketing

We currently have no sales, marketing or distribution capabilities, as such, in order to commercialize any of our drug candidates. We do, however, have worldwide commercialization rights for all of our development programs. We intend to develop these capabilities internally as needed and through collaboration with third parties.

Competition

The development and commercialization of new drugs is highly competitive. We will face competition with respect to all drug candidates we may develop or commercialize in the future from pharmaceutical and biotechnology companies worldwide. The key competitive factors affecting the success of any approved product will be its efficacy, safety profile, price, method of administration and level of promotional activity. The efficacy and safety profile of our drug candidates relative to competitors will depend upon the results of our clinical trials and experience with the approved product in the commercial marketplace. For risks associated with competition, see "Risks Related to Our Industry—Our market is subject to intense competition..." under "Risk Factors" below in Part I, Item 1A of this Annual Report on Form 10-K.

Patents and Proprietary Rights

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

As of January 31, 2013, our patent portfolio had a total of 843 patents and patent applications worldwide, including specific patent filings with claims to the composition-of-matter and methods of use of ganetespib and elesclomol. We own or have exclusively licensed a total of 79 issued U.S. patents and 99 U.S. patent applications, as well as 665 foreign counterparts to these patents and patent applications.

With respect to our Hsp90 inhibitor program, we have 80 issued U.S. and foreign patents, and 150 pending U.S. and foreign counterpart patent applications. Any U.S. or foreign patent that issues covering ganetespib will expire no earlier than 2025. Our Hsp90 inhibitor patent portfolio covers ganetespib and structurally related analogs, pharmaceutical compositions, and methods for treating

cancer. Additionally, we have multiple U.S. and corresponding foreign patent applications directed to other Hsp90 inhibitors.

With respect to elesclomol, we have 2 issued U.S. patents that claim the chemical structure of elesclomol that expire no earlier than 2022. Both of these issued U.S. patents also claim related chemical structures, pharmaceutical compositions, and methods for treating a subject with cancer. In addition, we have an issued U.S. patent claiming the salt form of elesclomol that expires no earlier than 2025.

We have pending U.S. patent applications covering compositions-of-matter, methods of treatment and other aspects of our programs for STA-9584, our IL-12/23 inhibitors and our CRACM ion channel inhibitors. Counterpart filings to these patents and patent applications have been made in a number of other jurisdictions, including Europe and Japan. The patent term of our U.S. patents may potentially be extended under applicable laws or regulations, such as the Patent Term Restoration Act.

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

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing and export and import of products such as those we are developing. Our drug candidates must be approved by the FDA through the new drug application, or NDA, process before they may be legally marketed in the United States.

United States Government Regulation

NDA Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or the FDCA, and implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative or judicial sanctions. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning letters;
- product seizures;
- total or partial suspension of production or distribution; or
- injunctions, fines, civil penalties or criminal prosecution.

Any agency regulatory or judicial enforcement action could have a material adverse effect on us. The process of obtaining regulatory approvals and the subsequent substantial compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests and animal studies according to Good Laboratory Practices, or GLPs;
- submission of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices, or GCPs, to establish the safety and efficacy of the proposed drug for its intended use;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of sites related to the manufacture, testing, release, distribution and management of commercial product to assess compliance with cGMPs and to assure that the facilities, methods and controls are adequate to preserve the drugs identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some preclinical or nonclinical testing may continue even after the IND is submitted. In addition to including the results of the preclinical studies, the IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, specifically places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND, and may affect one or more specific studies or all studies conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCP regulations, which ensures, among other things, that each research subject provides informed consent. Further, an institutional review board, or IRB, at each institution participating in the clinical trial must review and approve the protocol for any clinical trial and the related consent form before the clinical trial commences at that institution. The IRB also has ongoing monitoring responsibilities with respect to each active trial. Each new clinical protocol and any amendments must be submitted to the FDA as part of the IND and to each IRB. Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently in other situations including the occurrence of serious adverse events.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1.* The drug is initially introduced into healthy human subjects or patients with the disease and tested for safety, dosage tolerance, pharmacokinetics, pharmacodynamics, absorption, metabolism, distribution and elimination. In the case of some products for severe or life-threatening diseases, especially when the product may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- *Phase 2.* Clinical trials are initiated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

- *Phase 3.* Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling.

Phase 1, Phase 2, and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. In addition, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements, in accordance with the clinical protocol, or if the drug has been associated with unexpected serious harm to patients.

During the development of a new drug, sponsors are given an opportunity to meet with the FDA at certain points. These points are: prior to submission of an IND, at the end of Phase 1 or Phase 2, and before an NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice, and for the sponsor and FDA to reach agreement on the next phase of development. Sponsors typically use the end of Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support approval of the new drug. If a Phase 2 clinical trial is the subject of discussion at an end of Phase 2 meeting with the FDA, a sponsor may be able to request a Special Protocol Assessment, the purpose of which is to reach agreement with the FDA on the design of the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim. If such an agreement is reached, it will be documented and made part of the administrative record, and it will be binding on the FDA unless public health concerns unrecognized at the time of protocol assessment are evident, and may not be changed except under a few specific circumstances.

On occasion, the FDA may suggest or the sponsor of a clinical trial may decide to use an independent data monitoring committee, or DMC, to provide advice regarding the continuing safety of trial subjects and the continuing validity and scientific merit of a trial. In 2006, the FDA published a final Guidance for Clinical Trial Sponsors on the Establishment and Operations of Clinical Trial Data Monitoring Committees in which it describes the types of situations in which the use of a DMC is appropriate and suggests how a DMC should be established and operate. DMCs evaluate data that may not be available to the sponsor during the course of the study to perform interim monitoring of clinical trials for safety and/or effectiveness and consider the impact of external information on the trial. They often make recommendations to the sponsor regarding the future conduct of the trial.

Concurrent with clinical trials, companies usually complete additional animal safety studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and the manufacturer must develop methods for testing the quality, purity and potency of the final drugs. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf-life.

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, results of chemical studies and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept a NDA for filing. In this event, the

NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

Once the NDA is accepted for filing, the FDA begins an in-depth review. NDAs receive either standard or priority review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. The FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data. Even if such data are submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested.

The FDA may require, as a condition of approval, restricted distribution and use, enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, pre-approval of promotional materials, restrictions on direct-to-consumer advertising or commitments to conduct additional research post-approval. The FDA will issue a complete response letter if the agency decides not to approve the NDA in its present form. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.

Satisfaction of FDA requirements or similar requirements of foreign regulatory authorities typically takes at least several years and the actual time required may vary substantially, based upon, among other things, the indication and the type, complexity and novelty of the product. Government regulation may delay or prevent marketing of potential products for a considerable period of time and impose costly requirements upon us. Success in early stage clinical trials does not assure success in later stage clinical trials. Data obtained from clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval on a timely basis, or at all. Even if a product receives regulatory approval, the approval may be significantly limited to specific diseases and dosages or the indications for use may otherwise be limited, which could restrict the commercial application of the product. Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. Delays in obtaining, or failures to obtain, regulatory approvals for any drug candidate could substantially harm our business and cause our stock price to drop significantly. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

Expedited Review and Approval

The FDA has various programs, including Fast Track, priority review, and accelerated approval, which are intended to expedite or simplify the process for reviewing drugs, and/or provide for approval on the basis of surrogate endpoints. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development, and expedite the review of drugs to treat serious diseases and fill an unmet medical need. Priority review is designed to give drugs that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review

within six months as compared to a standard review time of 10 months. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review. Accelerated approval provides an earlier approval of drugs to treat serious diseases, and that fill an unmet medical need based on a surrogate endpoint, which is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform post-marketing clinical trials.

In the recently enacted Food and Drug Administration Safety and Innovation Act, or FDASIA, Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of products under accelerated approval. The law requires the FDA to issue related draft guidance within a year after the law's enactment and also promulgate confirming regulatory changes.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drug candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND, and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages, or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States and for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for this type of disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Orphan drug exclusivity, however, also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA or if our drug candidate is determined to be contained within the competitor's product for the same indication or disease.

Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act, or BPCA, certain drugs may obtain an additional six months of exclusivity, if the sponsor submits information requested in writing by the FDA, or a Written Request, relating to the use of the active moiety of the drug in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a drug in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

We have not received a Written Request for such pediatric studies, although we may ask the FDA to issue a Written Request for such studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles, and submit reports of the studies. A Written Request may include studies for indications that are not currently in the labeling if the FDA determines that such information will benefit the public health. The FDA will accept the reports upon its determination that the studies were conducted in accordance with and are responsive to the original Written Request or commonly accepted scientific principles, as appropriate, and that the reports comply with the FDA's filing requirements.

In addition, the Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for most drugs and biologicals, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, biologics license application and supplements thereto, must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

As part of the FDASIA, Congress made a few revisions to BPCA and PREA, which were slated to expire on September 30, 2012, and made both laws permanent.

Post-approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs.

Any drug products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences with the drug;
- providing the FDA with updated safety and efficacy information;
- drug sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes;
- complying with certain electronic records and signature requirements; and
- complying with FDA promotion and advertising requirements.

Drug manufacturers and their subcontractors are required to register their establishments with the FDA and some state agencies, and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP and other laws.

We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products. Future FDA and state inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, a company may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is

compulsory for medicines produced by biotechnology or those medicines intended to treat AIDS, cancer, neurodegenerative disorders, or diabetes and optional for those medicines which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for approval by one or more "concerned" member states based on an assessment of an application performed by one member state, known as the "reference" member state. Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state does not recognize the marketing authorization, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states.

As in the United States, we may apply for designation of a product as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Orphan drugs in Europe enjoy economic and marketing benefits, including up to 10 years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product.

Reimbursement

Sales of our products will depend, in part, on the extent to which the costs of our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly challenging the prices charged for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the prices of drugs have been a focus in this effort. The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our drug candidates or a decision by a third-party payor to not cover our drug candidates could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operation and financial condition.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposes requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors have begun to follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors as well.

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

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the ACA) enacted in March 2010, isexpected to have a significant impact on the health care industry. The ACA is expected to expand coverage for the uninsured while at the same time contain overall healthcare costs. With regard to pharmaceutical products, among other things, the ACA is expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare D program. We cannot predict the impact of the ACA on pharmaceutical companies as many of the ACA reforms require the promulgation of detailed regulations implementing the statutory provisions which has not yet occurred. In addition, although the United States Supreme Court recently upheld the constitutionality of most of the ACA, some states have indicated that they intend to not implement certain sections of the ACA, and some members of the U.S. Congress are still working to repeal the ACA. These challenges add to the uncertainty of the legislative changes enacted as part of the ACA.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the European Union do not follow price structures of the United States and generally tend to be significantly lower.

Employees

As of December 31, 2012, we had 124 full time employees, including a total of 44 employees who hold M.D. or Ph.D. degrees. Ninety-two of our employees are primarily engaged in research and development activities, and 32 are primarily engaged in general and administrative activities. Our employees are not represented by any collective bargaining unit, and we believe our relations with our employees are good.

Company History and Available 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 Annual Report on Form 10-K. We have included our website address as a factual reference and do not intend it to be an active link to our website. Our trademarks include Synta Pharmaceuticals, our corporate logo and the GALAXY trial. Other service marks, trademarks and trade names appearing in this Annual Report on Form 10-K 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 section of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the Securities and Exchange Commission, or the SEC. You may also read and copy any document we file at the SEC's Public Reference Room at 100 F Street N.E., Washington, D.C. 20549. Please call 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

Item 1A. RISK FACTORS

If any of the following risks occurs, our business, business prospects, financial condition, results of operations, or cash flows could be materially harmed.

Risks Related to Our Financial Position and Need for Additional Capital

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

Since inception we have incurred significant operating losses and, as of December 31, 2012, we had an accumulated deficit of $461.2 million. We expect to continue to incur significant operating expenses and capital expenditures and anticipate that our expenses and losses may increase substantially in the foreseeable future as we:

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

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

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

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

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

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

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

We do not anticipate that we will generate product revenue in the foreseeable future, if at all. We expect our continuing operations to use cash over the next several years and such cash use may increase significantly from year to year. While we are engaged in multiple preliminary partnership discussions for each of our currently unpartnered programs, including ganetespib, elesclomol, STA-9584, CRACM inhibitors, and IL-12/23 inhibitors, which could result in one or more new partnership agreements that may include upfront payments and cost-sharing provisions, there is no guarantee we will be successful in entering into any such partnership agreements on commercially reasonable terms, if at all, or that we will receive any other revenue through these partnership efforts in the future. Based on our current operating levels, we expect our cash resources will be sufficient to fund operations into the second quarter of 2014. This estimate assumes that the timing and nature of activities contemplated

for 2013 will be conducted subject to the availability of sufficient financial resources. We continue to evaluate additional potential sources of funding, including partnership agreements, cost or risk-sharing arrangements, equity financings, use of our $28 million at-the-market issuance sales agreement with MLV and other sources.

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

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

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

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

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

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

On September 30, 2010, we entered into a $15 million loan and security agreement with General Electric Capital Corporation, or GECC, and one other lender, which we refer to herein as the GECC Term Loan. The GECC Term Loan is secured by substantially all of our assets, except our intellectual property. We have, however, granted GECC a springing security interest in our intellectual property in the event that we are not in compliance with certain cash burn covenants set forth in the agreement. In addition, the GECC Term Loan contains restrictive covenants, including the requirement for us to receive prior written consent of GECC to enter into loans, other than up to $4.0 million of equipment financing, restrictions on the declaration or payment of dividends, restrictions on acquisitions, and customary default provisions that include material adverse events, as defined therein. Our failure to comply with these covenants may result in the declaration of an event of default that, if not cured or waived, may result in the acceleration of the maturity of indebtedness outstanding under the GECC Term Loan, which would require us to pay all amounts outstanding. If an event of default occurs, we

may not be able to cure it within any applicable cure period, if at all. If the maturity of our indebtedness is accelerated, we may not have sufficient funds available for repayment or we may not have the ability to borrow or obtain sufficient funds to replace the accelerated indebtedness on terms acceptable to us or at all.

In March 2011, we entered into a $2 million loan and security agreement with Oxford Finance Corporation, or Oxford, which we refer to as the Oxford Term Loan. In December 2012, we entered into a loan modification agreement under which we may draw down up to an additional $0.6 million in equipment financing until May 31, 2013. As of December 31, 2012, noadditional equipment financing had been used. The Oxford Term Loan is secured by certain laboratory and office equipment, furniture and fixtures acquired through September 30, 2010. In connection with the Oxford Term Loan, Oxford and GECC entered into a Lien Subordination Agreement, whereby GECC granted Oxford a first priority perfected security interest in the loan collateral. The Oxford Term Loan contains restrictive covenants, including the requirement for us to receive the prior written consent of Oxford to enter into acquisitions in which we incur more than $2.0 million of related indebtedness, and customary default provisions that include material adverse events, as defined therein.

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

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

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

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

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

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

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

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

- the drug candidate may not prove to be safe and effective;
- the dosing of the drug candidate in a particular clinical trial may not be optimal;
- patients may die or suffer other adverse effects for reasons that may or may not be related to the drug candidate being tested;
- the results may not confirm the positive results of earlier clinical trials or preclinical studies; and
- the results may not meet the level of statistical significance or clinical benefit-to-risk ratio required by the FDA or other regulatory agencies for marketing approval.

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

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

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

that efficacy will be established or that new toxicities or other adverse effects will not be identified in the clinical trials that we conduct with this formulation. In addition, we have noted a relatively high pH in the final elesclomol infusion solution. Although there have been no reported concerns in the ongoing clinical trials using this solution, we cannot guarantee that there will be no complications related to the high pH of this solution in the future.

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

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

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

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

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

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

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

We cannot predict whether we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our other ongoing and planned clinical trials and negatively impact our ability to obtain regulatory approval for, and to market and sell, a particular drug candidate, including our clinical drug candidates, ganetespib and elesclomol, and our drug candidates that are still in preclinical studies, including STA-9584, our CRACM inhibitor candidates and our IL-12/23 inhibitor candidates:

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

Commercialization of our drug candidates may be delayed by the imposition of additional conditions on our clinical trials by the FDA or any foreign regulatory authority or the requirement of additional supportive studies by the FDA or any foreign regulatory authority. In addition, clinical trials require sufficient patient enrollment, which is a function of many factors, including the size of the target patient population, the nature of the trial protocol, the proximity of patients to clinical sites, the

availability of effective treatments for the relevant disease, the conduct of other clinical trials that compete for the same patients as our clinical trials, and the eligibility criteria for our clinical trials. Our failure to enroll patients in our clinical trials could delay the completion of the clinical trial beyond our expectations. In addition, the FDA could require us to conduct clinical trials with a larger number of subjects than we have projected for any of our drug candidates. We may not be able to enroll a sufficient number of patients in a timely or cost-effective manner. Furthermore, enrolled patients may drop out of our clinical trials, which could impair the validity or statistical significance of the clinical trials.

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

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

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

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

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

- restrictions on the products, manufacturers, or manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;

- product seizures or detentions;
- import bans;
- suspension or withdrawal of regulatory approvals;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new drug candidates or supplements to approved applications.

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

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

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

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

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

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

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

Our activities involve the controlled storage, use, and disposal of hazardous materials, including cytotoxic agents, genotoxic agents, infectious agents, corrosive, explosive and flammable chemicals, and various radioactive compounds. We are subject to federal, state, and local laws and regulations governing the use, manufacture, storage, handling, and disposal of these hazardous materials. Although we believe that our safety procedures for the handling and disposing of these materials comply with the

standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials.

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

Risks Related to Our Dependence on Third Parties

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

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

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

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

Our drug candidates require precise, high quality manufacturing. Failure by our contract manufacturers to achieve and maintain high manufacturing standards could result in patient injury or death, product recalls or withdrawals, delays or failures in testing or delivery, cost overruns, or other problems that could seriously hurt our business. Contract manufacturers may encounter difficulties involving production yields, quality control, and quality assurance. These manufacturers are subject to ongoing periodic unannounced inspection by the FDA and corresponding state and foreign agencies to ensure strict compliance with current Good Manufacturing Practice regulations, or cGMPs, and other applicable U.S. and foreign government regulations and standards. We periodically audit our contract

manufacturers responsible for supplying our clinical drug materials and have put quality agreements in place that we believe are appropriate for our materials. However, we do not have direct control over third party manufacturers' compliance with cGMPs and other standards and therefore, cannot provide assurance regarding such compliance.

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

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

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

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

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

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

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

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

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

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

Our drug development programs and potential commercialization of our drug candidates will require substantial additional cash to fund expenses. We own all rights to our two lead drug candidates, elesclomol and ganetespib, and are fully responsible for the associated development costs. Our strategy continues to include the potential of selectively collaborating with leading pharmaceutical and biotechnology companies to assist us in furthering development and potential commercialization of some of our drug candidates and research programs. We may enter into one or more of such collaborations in the future, especially for target indications in which the potential collaborator has particular therapeutic expertise or that involve a large, primary care market that must be served by large sales and marketing organizations or for markets outside of North America. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on acceptable terms, or at all. Even if we successfully enter into a collaboration, we cannot provide assurance that our partner will perform its contractual obligations or will not terminate the agreement. If that were to occur, we may have to curtail the development of a particular drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of our sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we will not be able to bring our drug candidates to market and generate product revenue.

Risks Related to Our Intellectual Property

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

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

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

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

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

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

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

- we or our licensors were the first to make the inventions covered by each of our pending patent applications;
- we or our licensors were the first to file patent applications for these inventions;

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

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

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

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

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

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

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

However, while it is our practice to conduct freedom to operate searches and analyses, we cannot guarantee that we have identified every patent or patent application that may be relevant to the

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

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

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

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

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

As is commonplace in our industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we have previously been subject to a claim by an alleged competitor that a prospective employee we sought to hire was bound by an ongoing non-competition obligation which prevented us from hiring this employee. We may be subject in the future to claims that our employees or prospective employees are subject to a continuing obligation to their former employers (such as non-competition or non-solicitation obligations) or claims that our employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Risks Related to the Commercialization of Our Drug Candidates

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

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

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

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

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

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

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

For example, the Medicare Prescription Drug Improvement and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation

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

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

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

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

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

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

The use of any of our drug candidates in clinical trials, and the sale of any approved products, might expose us to product liability claims. We currently maintain product liability insurance, and we monitor the amount of coverage we maintain as the size and design of our clinical trials evolve and adjust the amount of coverage we maintain accordingly. However, there can be no assurance that such insurance coverage will fully protect us against some or all of the claims to which we might become

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

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

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

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

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

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

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

In the event that we are found to have violated these laws or decide to settle a claim that we have done so, our business may be materially adversely affected as a result of any payments required to be

made, restrictions on our future operations or actions required to be taken, damage to our business reputation or adverse publicity in connection with such a finding or settlement or other adverse effects relating thereto. Additionally, even an unsuccessful challenge or investigation into our practices could cause adverse publicity, and be costly to respond to, and thus could harm our business and results of operations.

Risks Related to Our Industry

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

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

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

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

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

Competitive products may render our products obsolete or noncompetitive before we can recover the expenses of developing and commercializing our drug candidates. Furthermore, the development of new treatment methods and/or the widespread adoption or increased utilization of any vaccine for the diseases we are targeting could render our drug candidates noncompetitive, obsolete or uneconomical. If we successfully develop and obtain approval for our drug candidates, we will face competition based on the safety and effectiveness of our drug candidates, the timing of their entry into the market in relation to competitive products in development, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent position and other factors. If we successfully develop

drug candidates but those drug candidates do not achieve and maintain market acceptance, our business will not be successful.

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

Ganetespib. If approved, ganetespib may compete against the currently approved therapies for the treatment of various cancer types and other cancer treatments currently under development. In particular, ganetespib may compete with other agents under development that inhibit Hsp90, including retaspimycin hydrochloride (IPI-504), being developed by Infinity Pharmaceuticals, AUY922, KW-2478, being developed by Kyowa Hakko Kirin, AT13387, being developed by Astex Pharmaceuticals, Debio0932, being developed by Curis/Debiopharma, DS-2248, being developed by Daiichi Sankyo, SNX-5422, being developed by Esanex, and PU-H71, being developed by Samus Therapeutics, among others.

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

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

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

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

- Stelara, a fully human monoclonal antibody targeting the p40 subunit of IL-12 and IL-23, marketed by Johnson & Johnson and approved in the U.S. and Europe for the treatment of plaque psoriasis and in Japan for the treatment of plaque psoriasis and psoriatic arthritis. IL-12/23 inhibitors may also compete with briakinumab (ABT-874), a fully human anti-IL-12/23 monoclonal antibody being developed by Abbott Laboratories. Regulatory applications in the U.S. and Europe for approval of briakinumab for the treatment of psoriasis were withdrawn in January 2011 following regulatory feedback indicating that further data and analysis would be required.

- large-molecule, injectable TNF-antagonists, including, among others: Remicade, marketed by Johnson & Johnson; Enbrel, marketed by Amgen and Wyeth Pharmaceuticals; and Humira, marketed by Abbott Laboratories; and

- broadly immunosuppressive small molecule agents including corticosteroids and azathioprine.

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

- discover and develop medicines that are superior to other products in the market;

- attract high-quality scientific, product development, and commercial personnel;

- obtain patent and/or proprietary protection for our medicines and technologies;
- obtain required regulatory approvals;
- selectively commercialize certain drug candidates in indications treated by specialist physicians; and
- selectively partner with pharmaceutical companies in the development and commercialization of certain drug candidates.

Risks Related to Employee Matters and Managing Growth

We may be unsuccessful in retaining certain key personnel.

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

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

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

Risks Related to Our Common Stock

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

Prior to our February 2007 initial public offering, there was not a public market for our common stock. There is a limited history on which to gauge the volatility of our stock price; however, since our

common stock began trading on The NASDAQ Global Market on February 6, 2007 through December 31, 2012, our stock price has fluctuated from a low of $1.20 to a high of $11.25. Furthermore, the stock market has recently experienced significant volatility, particularly with respect to pharmaceutical, biotechnology, and other life sciences company stocks. The volatility of pharmaceutical, biotechnology, and other life sciences company stocks often does not relate to the operating performance of the companies represented by the stock. Some of the factors that may cause the market price of our common stock to fluctuate include:

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

These and other external factors may cause the market price and demand for our common stock to fluctuate substantially, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In addition, in the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If any of our stockholders

brought a lawsuit against us, we could incur substantial costs defending the lawsuit. Such a lawsuit could also divert the time and attention of our management.

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

Our directors and executive officers, together with their affiliates and related persons, beneficially own, in the aggregate, approximately 40.5% of our outstanding common stock. These stockholders, if acting together, may have the ability to determine the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation, or sale of all or substantially all of our assets. In addition, these persons, acting together, may have the ability to control the management and affairs of our company. Accordingly, this concentration of ownership may harm the market price of our common stock by:

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

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

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

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

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

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

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

Item 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

Item 2. PROPERTIES

Our operations are based primarily in Lexington, Massachusetts, which is located approximately 10 miles west of Boston, Massachusetts. We currently lease a total of 76,580 square feet of office and laboratory space, including 61,580 square feet in Lexington and 15,000 square feet in the neighboring town of Bedford, Massachusetts. We lease the following properties:

Location	Approximate Square Feet	Use	Lease Expiration Date
45 Hartwell Avenue Lexington, Massachusetts	34,520	Office and Laboratory	November 2016
125 Hartwell Avenue Lexington, Massachusetts	27,060	Office and Laboratory	November 2016
45 - 47 Wiggins Avenue Bedford, Massachusetts	15,000	Office and Laboratory	October 2016

Item 3. LEGAL PROCEEDINGS

We are currently not a party to any material legal proceedings.

Item 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

Item 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock is traded on The NASDAQ Global Market under the symbol "SNTA." The following table sets forth the high and low sales prices of our common stock as quoted on The NASDAQ Global Market for the periods indicated.

2011:	High	Low
First Quarter	$ 6.93	$ 4.26
Second Quarter	6.27	4.30
Third Quarter	5.23	3.25
Fourth Quarter	5.15	3.02

2012:	High	Low
First Quarter	$ 5.74	$ 4.03
Second Quarter	8.50	3.57
Third Quarter	8.54	5.35
Fourth Quarter	9.85	6.53

Stockholders

As of March 8, 2013, there were approximately 63 stockholders of record of the 69,054,951 outstanding shares of our common stock.

Dividends

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.

Unregistered Sales of Securities

None.

Issuer Purchases of Equity Securities

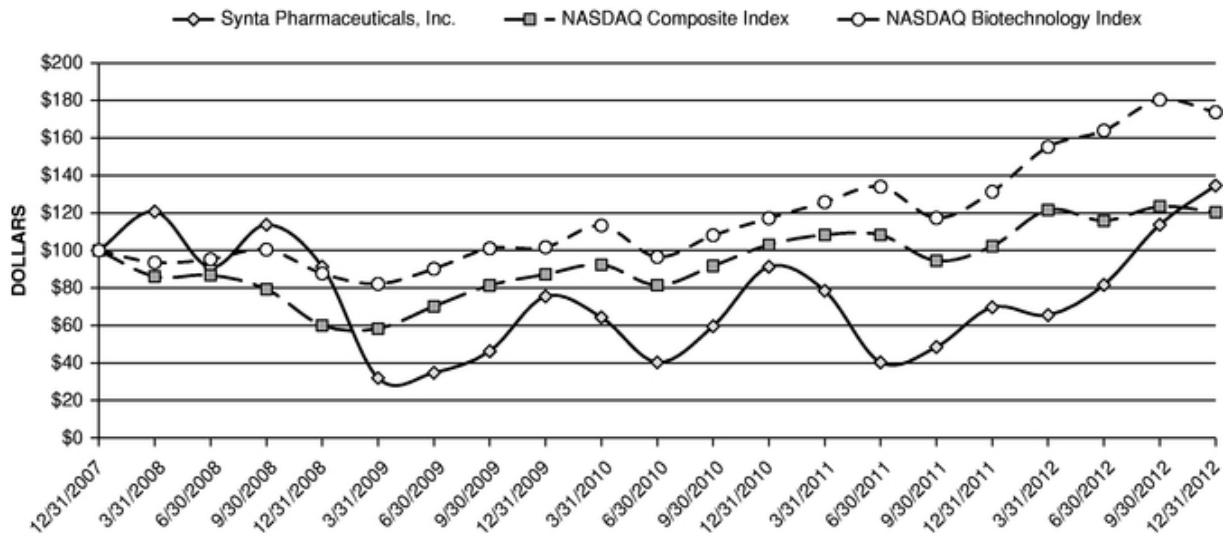
In November 2012, we repurchased 3,969 shares as part of the settlement of tax withholding obligations by a participant under our Amended and Restated 2006 Stock Plan. The following table sets forth repurchases that we made for the quarter ended December 31, 2012:

Period	Total Number of SharesPurchased	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number (or Approximate Dollar Value) of Shares that May Yet Be Purchased Under the Plans or Programs
October 1, 2012 - October 30, 2012	N/A	N/A	N/A	N/A
November 1, 2012 - November 30, 2012	3,969	$ 8.21	N/A	N/A
December 1, 2012 - December 31, 2012	N/A	N/A	N/A	N/A
Total	3,969	$ 8.21	N/A	N/A

Stock Performance Graph

The following graph compares the cumulative total stockholder return on our common stock from December 31, 2007 (the first trading date following our initial public offering) to December 31, 2012 with the cumulative total return of (i) the NASDAQ Composite Index and (ii) the NASDAQ Biotechnology Index. This graph assumes the investment of $100.00 on December 31, 2007 in our common stock, the NASDAQ Composite Index and the NASDAQ Biotechnology Index, and assumes any dividends are reinvested. We have not paid any dividends on our common stock, and we do not include dividends in the representation of our performance. The stock price performance on the graph below does not necessarily indicate future price performance.

COMPARISON OF CUMULATIVE TOTAL RETURN
SYNTA PHARMACEUTICALS CORP., NASDAQ COMPOSITE INDEX
AND NASDAQ BIOTECHNOLOGY INDEX



ASSUMES $100 INVESTED ON DEC. 31, 2007
ASSUMES DIVIDEND REINVESTED
FISCAL YEAR ENDED DEC. 31, 2012

The information in this section shall not be deemed "soliciting material" or to be "filed" with the Securities and Exchange Commission, and is not to be incorporated by reference in any filing of Synta Pharmaceuticals Corp. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of this Annual Report on Form 10-K and irrespective of any general incorporation language in those filings.

Item 6. SELECTED FINANCIAL DATA

The following table sets forth our selected consolidated financial data and has been derived from our audited consolidated financial statements. Consolidated balance sheets as of December 31, 2012 and 2011, as well as consolidated statements of operations for the years ended December 31, 2012, 2011, and 2010, and thereports thereon are included elsewhere in this Annual Report on Form 10-K. The information below should be read in conjunction with our audited consolidated financial

statements (and notes thereon) and "Management's Discussion and Analysis of Financial Condition and Results of Operations," included below in Item 7.

	Years ended December 31,				
	2012	2011	2010	2009	2008
	(all amounts in thousands except per share data)				
Consolidated Statement of Operations Data:					
Revenues:					
License and milestone revenue(1)	$ —	$ 6,731	$ 4,572	$ 125,701	$ 8,513
Cost sharing reimbursements, net	—	—	9,253	18,544	(5,898)
Grant revenue	147	853	978	—	—
Total revenues	147	7,584	14,803	144,245	2,615
Operating expenses:					
Research and development	49,412	41,464	40,252	51,054	81,581
General and administrative	11,676	11,552	11,449	12,651	14,742
Restructuring	—	—	—	1,236	—
Total operating expenses	61,088	53,016	51,701	64,941	96,323
Income (loss) from operations	(60,941)	(45,432)	(36,898)	79,304	(93,708)
Other (expense) income, net	(1,849)	(1,948)	(569)	(216)	1,090
Net income (loss)	$ (62,790)	$ (47,380)	$ (37,467)	$ 79,088	$ (92,618)
Net income (loss) per common share:					
Basic	$ (1.06)	$ (1.00)	$ (0.93)	$ 2.33	$ (2.75)
Diluted	$ (1.06)	$ (1.00)	$ (0.93)	$ 2.32	$ (2.75)
Weighted-average common shares outstanding:					
Basic	59,411	47,198	40,365	33,888	33,736
Diluted	59,411	47,198	40,365	34,119	33,736

(1) In October 2007, we entered into the GSK Agreement with GSK for elesclomol which was terminated effective September 2009, resulting in accelerated recognition of $114.6 million of previously deferred revenue in the third quarter of 2009. In December 2008, we entered into the Roche Agreement with Roche for our CRACM inhibitor program. Roche provided written notification of termination in November 2011, resulting in accelerated recognition of $2.1 million of previously deferred revenue in the fourth quarter of 2011. See Notes 2 and 8 in the accompanying consolidated financial statements.

	As of December 31,				
	2012	2011	2010	2009	2008
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 100,599	$ 39,725	$ 50,973	$ 44,155	$ 73,563
Working capital	77,899	25,138	34,784	28,105	57,898
Total assets	103,017	42,324	54,067	48,910	97,253
Capital lease obligations, net of current portion	1	14	26	799	2,012
Term loans, net of current portion	4,464	12,388	11,667	—	—
Common stock and additional paid-in capital	536,284	413,201	374,532	338,494	333,865
Accumulated deficit	(461,220)	(398,430)	(351,050)	(313,583)	(392,671)
Total stockholders' equity (deficit)	75,066	14,774	23,479	24,911	(58,791)

Item 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Management's Discussion and Analysis of Financial Condition and Results of Operations should be read together with the consolidated financial statements, related notes and other financial information included elsewhere in this Annual Report on Form 10-K.

Overview

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

We were incorporated in March 2000 and commenced operations in July 2001. Since that time, we have been principally engaged in the discovery and development of novel drug candidates. As of December 31, 2012, we have funded our operations principally with $465.2 million in net proceeds from private and public offerings of our equity, as well as $17 million in gross proceeds from two term loans, including $15 million from a term loan that was executed in September 2010 with General Electric Capital Corporation, or GECC, and one other lender, and $2 million from a term loan that was executed in March 2011 with Oxford Finance Corporation, or Oxford.

In January and February 2012, we raised approximately $33.0 million in net proceeds from the sale of an aggregate of 8,050,000 shares of our common stock in a public offering at a public offering price of $4.40 per share, including 7,000,000 shares in the initial closing in January 2012 and 1,050,000 shares in a second closing in February 2012 following the full exercise of the over-allotment option granted to the underwriters. In July 2012, we raised approximately $25.8 million in net proceeds from a registered direct offering of 3,976,702 shares of our common stock at a price of $6.49 per share to certain directors, including our largest stockholder. In December 2012, we raised approximately $59.8 million in net proceeds from a registered direct offering of 7,000,000 shares of our common stock at a price of $8.60 per share to investors and certain directors, including our largest stockholder.

On May 2, 2012, as amended, we entered into an at-the-market issuance sales agreement, or Sales Agreement, with MLV & Co. LLC, or MLV, pursuant to which we may issue and sell shares of our common stock having an aggregate offering price of up to $28 million from time to time, at our option, through MLV as our sales agent, subject to certain terms and conditions. To date, no shares have been sold under the Sales Agreement.

In addition to raising capital from financing activities, we have also received substantial capital from partnering activities. In October 2007, we entered into a global collaborative development, commercialization and license agreement with GlaxoSmithKline, or GSK, for the joint development and commercialization of elesclomol. This collaboration was terminated in September 2009. In December 2008, we entered into a collaborative license agreement with Hoffman-La Roche, or Roche, for our CRACM inhibitor program. This collaboration was terminated effective on February 16, 2012. As of December 31, 2012, we have received $167.2 million in nonrefundable partnership payments under these agreements with GSK and with Roche, including $96 million in upfront payments, $50 million in operational milestones and $21.2 million in research and development funding. As of December 31, 2012, these nonrefundable partnership payments together with the cash proceeds from equity financings, the term loans from GECC and Oxford, and the exercise of common stock warrants and options, provided aggregate cash proceeds of approximately $652.5 million. We have also generated funds from government grants, equipment lease financings and investment income. We are engaged in

preliminary partnership discussions for a number of our programs, which may provide us with additional financial resources if consummated.

We have devoted substantially all of our capital resources to the research and development of our drug candidates. Since our inception, we have had no revenues from product sales. As of December 31, 2012, we had an accumulated deficit of $461.2 million. We expect to incur significant operating losses for the foreseeable future as we advance our drug candidates from discovery through preclinical development and clinical trials, and seek regulatory approval and eventual commercialization. We will need to generate significant revenues from product sales to achieve future profitability and may never do so.

Oncology Programs

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

Ganetespib (Hsp90 Inhibitor)

Ganetespib is a potent, synthetic, small molecule inhibitor of Hsp90, a chaperone protein that is essential to the function of certain other proteins, such as tyrosine kinases and transcription factors that drive the growth, proliferation, and survival of many different types of cancer. Ganetespib is currently being evaluated in a broad range of clinical trials both in combination with other therapies and as a single agent.

In clinical trials to date, ganetespib has shown encouraging evidence of clinical activity, including, when used as monotherapy, prolonged tumor shrinkage in patients who have progressed after, or failed to respond to, treatment with commonly-used drugs for these tumors, and in combination with chemotherapy where improvements in overall survival have been seen in a randomized study. Ganetespib is currently being evaluated in a broad range of cancer clinical trials including our 800-patient GALAXY NSCLC program in combination with docetaxel chemotherapy, and as monotherapy in certain genetically-defined targeted patient populations. A favorable safety profile has been consistently observed across clinical trials, involving over 700 patients treated with ganetespib to date. 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.

Ganetespib Mechanism of Action

Ganetespib potently inhibits Hsp90, a chaperone protein required for the proper folding and activation of numerous client proteins, particularly kinases, that play critical roles in tumor cell growth, differentiation and survival. A number of sensitive Hsp90 client proteins, such as ALK, HER2, AR, mutant BRAF and EGFR, have been implicated as oncogenic drivers in a variety of human tumors, including lung, breast, prostate and melanoma. Moreover, many client proteins are the targets of marketed cancer drugs such as Avastin, Erbitux, Gleevec, Herceptin, Nexavar, Sutent, Tarceva, Votrient, Xalkori, and Zelboraf.

Ganetespib is a novel small molecule that is 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. Results published in *Molecular Cancer Therapeutics* in December 2011 highlighted certain physicochemical properties of ganetespib we believe contribute to its improved safety and activity relative to other Hsp90 inhibitors. These properties include smaller size, greater potency in inhibiting Hsp90, improved ability to passively enter cells,

absence of a molecular component believed to cause liver toxicity, and the ability to penetrate deep into tumor tissue.

Because of the broad spectrum of biological activity conferred by ganetespib treatment, an additional approach has been to combine this agent with standard of care chemotherapeutics or other molecularly-targeted agents. In this regard, we have demonstrated a clear capacity of ganetespib to augment the cytotoxic activity of DNA damaging chemotherapeutics in multiple models. In addition, our data suggest that many relevant client proteins affected by ganetespib within this context are implicated in other critical tumorigenic processes, such as metastasis and angiogenesis. Prior work has established that regulators of tumor metastasis, such as the transcription factor HIF-1alpha, and regulators of angiogenesis, including VEGF and related receptors, are all down-regulated by ganetespib.

Ganetespib Clinical Trials

We are sponsoring four principal ongoing trials evaluating ganetespib activity:

- GALAXY-1: a 300-patient global, randomized Phase 2b/3 trial designed to evaluate ganetespib in combination with docetaxel versus docetaxel alone as second-line therapy in advanced NSCLC patients with adenocarcinoma histology,

- GALAXY-2: a 500-patient, global, randomized, confirmatory Phase 3 clinical trial evaluating ganetepsib plus docetaxel vs. docetaxel alone for the treatment of second-line advanced adenocarcinoma NSCLC, as with GALAXY-1. Results from an interim analysis of the GALAXY-1 trial conducted in September 2012 were used to inform the design of GALAXY-2, enriching for those patients who showed enhanced clinical benefit from treatment with ganetespib in GALAXY-1,

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

- ENCHANT: a Phase 2 trial evaluating ganetespib monotherapy in patients with newly diagnosed HER2+ and triple-negative metastatic breast cancer.

NSCLC

In a June 2012 we reported top line results from a planned interim analysis of GALAXY-1. The analysis was planned for when approximately 50% of patients had been enrolled. At the time of this analysis, a total of 114 adenocarcinoma and 69 non-adenocarcinoma patients had been enrolled.

On September 29, 2012, we reported results from the second interim efficacy analysis at the European Society for Medical Oncology (ESMO) 2012 Congress. Overall survival results are described in the table below. Median survival for the docetaxel control arm in both the intent to treat (ITT) and the 6-month follow up groups was consistent with comparable historical results. Median survival had not yet been reached for the combination arm.

Overall survival, all adenocarcinoma patients

	All patients in database (N=172)	All patients enrolled more than 6 months prior to data cutoff (N=77)
HR	0.688	0.568
C.I. (90%)	(0.417, 1.135)	(0.312, 1.032)
p-Value	0.183	0.056
Median (D vs G+D)	7.4 mo vs. NR	7.4 mo vs NR

HR: Hazard ratio, C.I.: confidence interval, NR: not reached

Progression free survival was 2.8 months vs. 4.2 months (p=0.076) and overall response rate was 8% vs. 16% (p=0.078) for docetaxel vs. ganetespib plus docetaxel, respectively. All p-values are calculated using the 1-sided stratified log-rank test for survival endpoints and using Fisher's Exact test for response rate.

In November 2012, we participated in an End-of-Phase 2 (EOP2) meeting with the U. S. Food and Drug Administration (FDA) to review plans for the 500-patient, global, randomized Phase 3 GALAXY-2 clinical trial. We have incorporated comments from this meeting into the protocol, and expect enrollment to begin in the first quarter of 2013.

The GALAXY-2 trial will enroll adenocarcinoma patients with advanced NSCLC who have received one prior treatment for metastatic disease, and will randomize those patients 1:1 to treatment with docetaxel plus ganetespib, or docetaxel alone, as with GALAXY-1.

The same dose and schedule used in GALAXY-1 will be used in the Phase 3 GALAXY-2 trial. Patients on both arms will receive docetaxel generally for four to six 21-day cycles, as per standard practice at their treatment center. After completion of docetaxel treatment, patients on the ganetespib arm are eligible to continue to receive ganetespib monotherapy as maintenance treatment. The trial will be conducted in many of the 60 centers across Europe and North America that participated in the GALAXY-1 trial, together with approximately 60 additional centers.

Results from the interim analysis for GALAXY-1 were used to inform the eligibility criteria for the GALAXY-2 trial. GALAXY-2 will enroll patients who have progressed following treatment with one prior platinum-containing regimen of chemotherapy as first-line therapy, and who were diagnosed with metastatic disease at least six months prior to study entry.

The primary endpoint of GALAXY-2 will be overall survival. Two event-driven interim analyses of the overall survival primary endpoint of GALAXY-2 have been specified. Based on current projections and statistical assumptions, we expect these analyses, together with the final overall survival analysis, to occur in 2014.

In 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. Results presented at these meetings 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). To further characterize ganetespib activity in the ALK+ NSCLC treatment setting, we initiated the CHIARA trial in 2012 to evaluate ganetespib monotherapy in ALK+ NSCLC patients who have not been previously treated with a direct ALK inhibitor. We expect to use results from an initial phase of enrollment, which was completed in the first quarter of 2013, to inform our decision on whether to continue additional enrollment in this trial.

Preclinical results from experiments conducted in our laboratories have demonstrated synergy between ganetespib and crizotinib or other ALK inhibitors. These data support our view of future combination approaches with ganetespib and ALK inhibitors for treatment of ALK+ NSCLC. 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 patients with ALK+ NSCLC that have not been previously treated with an ALK inhibitor began enrolling patients at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York City in 2012.

Breast Cancer

In 2012, we initiated the ENCHANT trial designed to evaluate ganetespib monotherapy as first-line treatment for both metastatic HER2+ breast cancer and TNBC. Patients in both cohorts will be assessed at baseline and at week 3, 6, and 12 with a combination of PET and CT scans. The primary endpoint of this study is overall response rate at week 12. Up to 35 patients will be enrolled in each of the HER2+ and TNBC cohorts. We expect preliminary results from the ENCHANT trial in the first half of 2013.

In addition to evaluating monotherapy administration of ganetespib in breast cancer, we and our collaborators believe that combination therapy with ganetespib has promise. 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 clinical trials

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

- 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 in 2012;
- 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 in 2012;
- a trial evaluating both ganetespib monotherapy and the combination of ganetespib and bortezomib in multiple myeloma, which began enrolling patients in 2012 and is supported by a grant of up to $1 million by the Multiple Myeloma Research Foundation;
- a randomized trial evaluating the combination of ganetespib and low dose ara-C chemotherapy in elderly patients with acute myeloid leukemia (AML) being conducted at Cardiff University, which began enrolling patients in 2012; and
- a trial evaluating ganetespib in combination with pemetrexed and cisplatin in patients with malignant pleural mesothelioma, being sponsored by Cancer Research UK, which we expect to begin enrolling patients in the first half of 2013.

In addition, a European cooperative group plans to initiate a randomized trial comparing paclitaxel with and without ganetespib in patients with advanced ovarian cancer in 2013.

Elesclomol (Mitochondria-Targeting Agent)

Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death (apoptosis), in cancer cells through a novel mechanism: disrupting cancer cell mitochondrial metabolism. In preclinical experiments, anti-cancer activity of elesclomol has been shown to correlate with certain biomarkers, including lactate dehydrogenase (LDH), which can distinguish between active mitochondria (sufficient oxygen present) and inactive mitochondria (insufficient oxygen present). 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 Memorial Sloan-Kettering Cancer Center 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. The ovarian cancer trial has met the prespecified efficacy requirement to advance to stage 2 and full enrollment of the Phase 2 study, indicating potential activity in this difficult-to-treat patient population with limited treatment options.

STA-9584 (Vascular Disrupting Agent)

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

Our Inflammatory Disease Programs

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

CRACM Ion Channel Inhibitors

We have developed novel, small molecule inhibitors of CRACM ion channels expressed on immune cells. Our CRACM ion channel inhibitors have shown 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.

On November 16, 2011, we received notice from Roche of its election to terminate the Roche Agreement, which termination became effective on February 16, 2012. Roche's termination of the agreement falls under the "Termination for Convenience" clause of the agreement. 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

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

Financial Operations Overview

Revenue

We have not yet generated any product revenue and do not expect to generate any product revenue in the foreseeable future, if at all. Our revenues to date have been generated primarily through our former collaboration agreements with GSK and Roche. The terms of these agreements included payment to us of upfront license fees, milestone payments, research and development cost sharing and royalties. We will seek to generate revenue from product sales and from future collaborative or strategic relationships. In the future, we expect any revenue we generate will fluctuate from quarter-to-quarter as a result of the timing and amount of payments received and expenses incurred under future collaborations or strategic relationships, and the amount and timing of payments we receive upon the sale of our drug candidates, to the extent any are successfully commercialized.

Research and Development

Research and development expense consists of costs incurred in connection with developing and advancing our drug discovery technology and identifying and developing our drug candidates. We charge all research and development expenses to operations as incurred.

Our research and development expense consists of:

- internal costs associated with research, preclinical and clinical activities;
- payments to third party contract research organizations, investigative sites and consultants in connection with our preclinical and clinical development programs;
- costs associated with drug formulation and supply of drugs for clinical trials;
- personnel related expenses, including salaries, stock-based compensation, benefits and travel; and
- overhead expenses, including rent and maintenance of our facilities, and laboratory and other supplies.

We do not know if we will be successful in developing our drug candidates. We believe that accurately projecting total program-specific expenses through commercialization is not possible at this time. The timing and amount of these expenses will depend upon the costs associated with potential future clinical trials of our drug candidates, and any expansion of our research and development organization, regulatory requirements, advancement of our preclinical programs and product manufacturing costs, many of which cannot be determined with accuracy at this time based on the stage of development of our drug candidates. This is due to the numerous risks and uncertainties associated with the duration and cost of clinical trials, which vary significantly over the life of a project as a result of unanticipated events arising during clinical development, including with respect to:

- the number of clinical sites included in the trial;
- the length of time required to enroll suitable subjects;
- the number of subjects that ultimately participate in the trials; and
- the efficacy and safety results of our clinical trials and the number of additional required clinical trials.

Our expenditures are subject to additional uncertainties, including the terms and timing of regulatory approvals. In addition, we may obtain unexpected or unfavorable results from our clinical trials. We may elect to discontinue, delay or modify clinical trials of some drug candidates or focus on others. A change in the outcome of any of the foregoing variables in the development of a drug candidate could mean a significant change in the costs and timing associated with the development of that drug candidate. For example, if the FDA or other regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate, or if we experience significant delays in any of our clinical trials, we would be required to expend significant additional financial resources and time on the completion of clinical development. Additionally, future commercial and regulatory factors beyond our control will evolve and therefore impact our clinical development programs and plans over time.

In 2013, we anticipate that the overall costs under our ganetespib program will increase as we further advance clinical development of ganetespib, including the GALAXY-1, GALAXY-2, ENCHANT and CHIARA trials, and conduct non-clinical supporting activities.

Beyond our current lead drug candidates, we anticipate that we will select drug candidates and research projects for further development on an ongoing basis in response to their preclinical and clinical success, as well as commercial potential.

General and Administrative

General and administrative expense consists primarily of salaries and related expenses for personnel in executive, finance, business and commercial development, investor and medical community relations, human resources and administrative functions. Other costs include stock-based compensation costs, directors' and officers' liability insurance premiums, legal costs of pursuing patent protection of our intellectual property, fees for general legal, accounting, public-company requirements and compliance, and other professional services, as well as overhead-related costs not otherwise included in research and development. In 2013, under our current operating plan, we anticipate that our general and administrative expenses will remain at levels similar to 2012. General and administrative expenses may increase in 2013 if we significantly expand pre-commercial development and medical community relations.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reported periods. We are required to make estimates and judgments with respect to research contract accruals, the recoverability of long-lived assets, measurement of stock-based compensation and the periods of performance under collaborative research and development agreements. We base our estimates on historical experience, known trends and events, and various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources and the reported amounts of revenues and expenses. Actual results may differ from these estimates under different assumptions or conditions.

Marketable Securities

Marketable securities consist of investments in high-grade corporate obligations, and government and government agency obligations that are classified as available-for-sale. Since these securities are available to fund current operations they are classified as current assets on the consolidated balance sheets.

We adjust the cost of available-for-sale debt securities for amortization of premiums and accretion of discounts to maturity. We include such amortization and accretion in interest and investment income. Realized gains and losses and declines in value, if any, that we judge to be other-than-temporary on available-for-sale securities are reported in interest and investment income. To determine whether an other-than-temporary impairment exists, we consider whether we intend to sell the debt security and, if we do not intend to sell the debt security, we consider available evidence to assess whether it is more likely than not that it will be required to sell the security before the recovery of our amortized cost basis. During the years ended December 31, 2012, 2011 and 2010, we determined that no securities were other-than-temporarily impaired.

Marketable securities are stated at fair value, including accrued interest, with their unrealized gains and losses included as a component of accumulated other comprehensive loss, which is a separate component of stockholders' equity. The fair value of these securities is based on quoted prices and observable inputs on a recurring basis. Realized gains and losses are determined on the specific identification method. During the years ended December 31, 2012, 2011 and 2010, we recorded no realized gains or losses on marketable securities.

Revenue Recognition

Collaboration and License Agreements

Our principal source of revenue to date has been generated from former collaborative research and development agreements with Roche and GSK, which included upfront license payments, development milestones, reimbursement of research and development costs, and potential profit sharing payments, commercialization and sales-based milestones and royalties. The application of accounting rules requires subjective analysis and requires management to make estimates and assumptions about whether deliverables within multiple-element arrangements are separable from the other aspects of the contractual arrangement into separate units of accounting and to determine the fair value to be allocated to each unit of accounting.

For multiple-element arrangements entered into or materially modified after January 1, 2011, we follow the provisions of ASU No. 2009-13 *Multiple-deliverable Revenue Arrangements (*ASU No. 2009-13). This standard addresses the determination of the unit(s) of accounting for multiple-element arrangements and how the arrangement's consideration should be allocated to each unit of accounting.

Pursuant to this standard, each required deliverable is evaluated to determine if it qualifies as a separate unit of accounting. For us this determination includes an assessment as to whether the deliverable has "stand-alone value" to the customer separate from the undelivered elements. The arrangement's consideration is then allocated to each separate unit of accounting based on the relative selling price of each deliverable. The estimated selling price of each deliverable is determined using the following hierarchy of values: (i) vendor-specific objective evidence of fair value, (ii) third-party evidence of selling price, and (iii) our best estimate of the selling price (BESP). The BESP reflects our best estimate of what the selling price would be if the deliverable was regularly sold by it on a stand-alone basis. We expect, in general, to use BESP for allocating consideration to each deliverable in future collaboration agreements. In general, the consideration allocated to each unit of accounting is then recognized as the related goods or services are delivered limited to the consideration not contingent upon future deliverables.

Effective January 1, 2011, we adopted ASU No. 2009-13 which codified a method of revenue recognition that has been common practice. Under this method, contingent consideration from research and development activities that is earned upon the achievement of a substantive milestone is recognized in its entirety in the period in which the milestone is achieved. At the inception of each arrangement that includes milestone payments, we evaluate whether each milestone is substantive. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. From the effective date of the adoption of this standard, we did not achieve any developmental, commercial or sales-based milestones pursuant to its research and collaboration agreement with Roche. Upon the effectiveness of the termination of the collaboration agreement with Roche on February 16, 2012, as more fully described in Note 8, we have no ongoing research and collaboration agreements under which milestones may be achieved.

Royalty revenues are based upon a percentage of net sales. Royalties from the sales of products will be recorded on the accrual basis when results are reliably measurable, collectibility is reasonably assured and all other revenue recognition criteria are met. Commercial and sales-based milestones,

which are based upon the achievement of certain agreed-upon sales thresholds, will be recognized in the period in which the respective sales threshold is achieved and collectibility is reasonably assured.

Accrued Expenses and Accrued Contract Research Liabilities

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves identifying services which have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date in our financial statements. Given our current business, the primary area of uncertainty concerning accruals which could have a material effect on our business is with respect to service fees paid to contract manufacturers in conjunction with the production of clinical drug supplies and to contract research organizations in connection with our preclinical studies and clinical trials. In connection with all of the foregoing service fees, our estimates are most affected by our understanding of the status and timing of services provided. The majority of our service providers, including contract research organizations, invoice us in arrears for services performed. In the event that we do not identify some costs which have begun to be incurred, or we under or over estimate the level of services performed or the costs of such services in a given period, our reported expenses for such period would be understated or overstated. We currently reflect the over or under accrual of expenses directly in our operations in the period the amount was determined.

Our arrangements with contract research organizations in connection with clinical trials often provide for payment prior to commencing the project or based upon predetermined milestones throughout the period during which services are expected to be performed. We recognize expense relating to these arrangements based on the various services provided over the estimated time to completion. The date on which services commence, the level of services performed on or before a given date, and the cost of such services are often determined based on subjective judgments. We make these judgments based upon the facts and circumstances known to us based on the terms of the contract and our ongoing monitoring of service performance. In the years ended December 31, 2012, 2011 and 2010, respectively, we had arrangements with multiple contract research organizations whereby these organizations commit to performing services for us over multiple reporting periods. We currently recognize and plan to continue to recognize the expenses associated with these arrangements based on our expectation of the timing of the performance of components under these arrangements by these organizations. Generally, these components consist of the costs of setting up the trial, monitoring the trial, closing the trial and preparing the resulting data. Costs related to patient enrollment in clinical trials are accrued as patients are enrolled in the trial.

With respect to financial reporting periods presented in this Annual Report on Form 10-K, and based on our receipt of invoices from our third party providers, the timing of our actual costs incurred have not differed materially from our estimated timing of such costs. In light of the foregoing, we do not believe our estimates of future expenses and our practice of making judgments concerning the accrual of expenses are reasonably likely to change in the future. There were no changes in our estimates and accruals for contract service fees that had a material effect on our net income (loss) for the years ended December 31, 2012, 2011 and 2010, respectively.

Stock-Based Compensation

We recognize stock-based compensation expense based on the fair value of stock options granted to employees, officers and directors. We use the Black-Scholes option pricing model as it is the most appropriate valuation method for our option grants. The Black-Scholes model requires inputs for risk-free interest rate, dividend yield, volatility and expected lives of the options. Expected volatility was principally based upon the weighted average historical volatility data of our common stock and the historical volatility data from several guideline public biotechnology companies similar in size and value to us that also have stock compensation plans with similar terms. We estimate the forfeiture rate based

on historical data. Based on an analysis of historical forfeitures, we have applied a forfeiture rate of 10% to all options that vest upon completion of the first year of service following the date of grant. The analysis is re-evaluated at least annually and the forfeiture rate is adjusted as necessary. The risk-free rate for periods within the expected life of the option is based on the U.S. Treasury yield curve in effect at the time of the grant. The expected lives for options granted represent the period of time that options granted are expected to be outstanding. We use the simplified method for determining the expected lives of options.

For awards with graded vesting, we allocate compensation costs on a straight-line basis over the requisite service period. We amortize the fair value of each option over each option's service period, which is generally the vesting period.

Our net income (loss) included compensation costs in the amount of $3.3 million, $3.4 million and $4.0 million for the years ended December 31, 2012, 2011 and 2010, respectively, and no income tax benefit related to our stock-based compensation arrangements for employee and non-employee awards. As of December 31, 2012, the total amount of unrecognized stock-based compensation expense was $7.9 million, which will be recognized over a weighted average period of 2.6 years.

Consolidated Results of Operations

Years Ended December 31, 2012, 2011 and 2010

Revenue

	Years Ended December 31,			2012 / 2011 Comparison		2011 / 2010 Comparison	
	2012	2011	2010	$	%	$	%
	(dollars in millions)						
Collaboration revenue							
License and milestone revenue—Roche	$ —	$ 6.7	$ 4.6	$ (6.7)	(100)%	$ 2.1	46%
	—	6.7	4.6	(6.7)	(100)%	2.1	46%
Cost sharing reimbursements, net—Roche	—	—	9.2	—	—%	(9.2)	(100)%
	—	—	9.2	—	—%	(9.2)	(100)%
Total collaboration revenue	—	6.7	13.8	(6.7)	(100)%	(7.1)	(51)%
Grant revenue	0.1	0.9	1.0	(0.8)	(89)%	(0.1)	(10)%
Total revenues	$ 0.1	$ 7.6	$ 14.8	$ (7.5)	(99)%	$ (7.2)	(49)%

Roche

Overview. In December 2008, as amended in February 2010, February 2011 and July 2011, we entered into a collaborative license agreement with Roche to discover, develop, and commercialize small-molecule drugs targeting CRACM channels and received a $16 million nonrefundable upfront payment from Roche in January 2009. Reimbursements of research and development costs to us by Roche were recorded as cost sharing revenue in the period in which the related research and development costs were incurred. The initial two-year research term concluded on December 31, 2010. On November 16, 2011, the Company received written notice of Roche's election to terminate the Roche Agreement, which termination became effective on February 16, 2012. (See Notes 2 and 8 in the accompanying consolidated financial statements.)

License and milestone revenue under the Roche Agreement decreased by $6.7 million in 2012 as compared to 2011 and increased by $2.1 million in 2011 as compared to 2010. In the fourth quarter of 2011, upon notification of Roche's election to terminate the Roche Agreement, we accelerated the recognition of approximately $2.1 million of remaining deferred revenue from the upfront payment because we had no remaining significant performance obligations.

Grant revenue

Grant revenue decreased by $0.8 million in 2012 as compared to 2011 and by $0.1 million in 2011 as compared to 2010. InMarch 2011, we received a grant from the DoD, in the approximate amount of $1 million, for the development of STA-9584 in advanced prostate cancer. We conducted work on this study during the one year grant period from April 2011 through March 2012. Reimbursements were based on actual costs agreed upon in the proposal (salary, fringe benefits, overhead, and direct costs such as materials and subcontractors). We recognized $147,000 and $853,000 of grant revenue under this grant in 2012 and 2011, respectively.

In November 2010, we were awarded approximately $1.0 million in grants under the Patient Protection and Affordable Care Act. We recognized approximately $1.0 million of grant revenue under these grants in 2010.

Research and Development Expense

	Years Ended December 31,			2012 / 2011 Comparison		2011 / 2010 Comparison	
	2012	2011	2010	$	%	$	%
	(dollars in millions)						
Clinical-stage drug candidates							
Ganetespib	$ 45.1	$ 30.1	$ 26.0	$ 15.0	50%	$ 4.1	16%
Elesclomol	0.7	3.8	2.9	(3.1)	(82)%	0.9	31%
Total clinical-stage drug candidates	45.8	33.9	28.9	11.9	35%	5.0	17%
CRACM	3.2	6.4	7.6	(3.2)	(50)%	(1.2)	(16)%
STA-9584	0.2	0.9	—	(0.7)	(78)%	0.9	—%
Other early stage programs	0.2	0.3	3.8	(0.1)	(33)%	(3.5)	(92)%
Total research and development	$ 49.4	$ 41.5	$ 40.3	$ 7.9	19%	$ 1.2	3%

Ganetespib

In 2012 as compared to 2011, costs incurred under our ganetespib program increased by $15.0 million, including increases of $5.3 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and $9.7 million for external costs. These increases were principally due to the near completion of patient enrollment in the GALAXY-1 trial that was initiated in the second quarter of 2011, start-up activities and clinical conduct in support of the CHIARA and ENCHANT trials that initiated in 2012, start-up activities in support of the GALAXY-2 trial that commenced in the fourth quarter of 2012 and increases related to the conduct of supporting drug supply and other non-clinical activities. We anticipate that the overall costs under our ganetespib program will increase in 2013 as we further advance clinical development, including the GALAXY-1, GALAXY-2, ENCHANT and CHIARA trials, and conduct non-clinical supporting activities.

In 2011 as compared to 2010, costs incurred under our ganetespib program increased by $4.1 million, including increases of $1.4 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and $2.7 million for external costs. Costs incurred in connection with the GALAXY-1 trial that was initiated in the second quarter of 2011, and the conduct of investigator-sponsored studies and supporting non-clinical activities were offset, in part, by lower costs in several company-sponsored clinical trials that were completed in 2011.

Elesclomol

In 2012 as compared to 2011, costs incurred under our elesclomol program decreased by $3.1 million, including decreases of $2.2 million for personnel-related costs, related research supplies,

operational overhead and stock compensation, and $0.9 million for external costs. These decreases were principally related to timing differences in the conduct of the Phase 2 clinical trial of elesclomol in combination with paclitaxel in ovarian cancer that is being conducted by the GOG and the Phase 1 clinical trial of elesclomol as a single agent in AML that were initiated in the first quarter of 2011, as well as supporting clinical drug supply. In 2013, we anticipate that the overall costs under our elesclomol program will remain at levels similar to 2012.

In 2011 as compared to 2010, costs incurred under our elesclomol program increased by $0.9 million, including increases of $0.5 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and $0.4 million for external costs. These increases were principally related to the commencement of patient enrollment in two clinical trials that were initiated in the fourth quarter of 2010, including a Phase 2 clinical trial of elesclomol in combination with paclitaxel in ovarian cancer that is being conducted by the GOG and a Phase 1 clinical trial of elesclomol as a single agent in AML, as well as supporting clinical drug supply.

CRACM

In 2012 as compared to 2011, costs incurred under our CRACM program decreased by $3.2 million, including a decrease of $3.5 million for personnel-related costs, related research supplies, operational overhead and stock compensation, offset by an increase of $0.3 million for external costs. This net decrease was the result of a lower investment in CRACM research following the conclusion of the Roche Agreement on February 16, 2012. In 2013, we anticipate that costs under the CRACM program may continue to decrease.

In 2011 as compared to 2010, costs incurred under our CRACM program decreased by $1.2 million, including decreases of $1.1 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and $0.1 million for external costs. These decreases were the result of a lower investment in CRACM research following the conclusion on December 31, 2010 of the two-year research term under the Roche Agreement.

STA-9584

In 2012 as compared to 2011, costs incurred under our STA-9584 program decreased by $0.7 million, including decreases of $0.2 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and $0.5 million for external costs. In March 2011, we received a grant from the DoD, in the approximate amount of $1 million, for the development of STA-9584 in advanced prostate cancer. We conducted work on this study during the one year grant period from April 2011 through March 2012. As our main focus continues to be advancing our ganetespib program, additional investments in our STA-9584 program are dependent upon obtaining funding from additional grants or partnerships.

In 2011 as compared to 2010, costs incurred under our STA-9584 program increased by $0.9 million, including increases of $0.3 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and $0.6 million for external costs. In March 2011, we received a $1 million grant from the DoD for the development of STA-9584 in advanced prostate cancer and initiated work on this study in the second quarter of 2011.

Early-stage programs

In 2012 as compared to 2011, costs incurred under our other early-stage programs decreased by $0.1 million principally due to a decrease of $0.1 million for external costs.

In 2011 as compared to 2010, costs incurred under our other early-stage programs decreased by $3.5 million principally due to decreases of $3.3 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and $0.2 million for external costs.

General and Administrative Expense

	Years Ended December 31,			2012 / 2011 Comparison		2011 / 2010 Comparison	
	2012	2011	2010	$	%	$	%
	(dollars in millions)						
General and administrative	$ 11.7	$ 11.5	$ 11.4	$ 0.2	2%	$ 0.1	1%

In 2012 as compared to 2011, the $0.2 million increase in general and administrative expense principally resulted from an increase of $0.8 million for personnel-related costs, related overhead and stock compensation, offset by a $0.6 million net decrease in external professional fees. In 2013, under our current operating plan, we anticipate that our general and administrative expenses will remain at levels similar to 2012. General and administrative expenses may increase in 2013 if we significantly expand pre-commercial development and medical community relations.

In 2011 as compared to 2010, the $0.1 million increase in general and administrative expense principally resulted from a decrease of $0.2 million for personnel-related costs, related overhead and stock compensation, offset by a $0.3 million increase in net external professional fees.

Interest Expense, net

	Years Ended December 31,			2012 / 2011 Comparison		2011 / 2010 Comparison	
	2012	2011	2010	$	%	$	%
	(dollars in millions)						
Interest expense, net	$ 1.8	$ 1.9	$ 0.6	$ (0.1)	(5)%	$ 1.3	217%

In 2012 as compared to 2011, interest expense decreased due to the commencement of principal payments in July 2012 under the GECC Term Loan. In 2013 as compared to 2012, we anticipate that interest expense will continue to decrease as principal continues to be paid under the current terms of the GECC Term Loan agreement.

In 2011 as compared to 2010, interest expense increased by $1.3 million principally due to interest expense in connection with the GECC Term Loan executed in September 2010 and the Oxford Term Loan executed in March 2011, offset, in part, by lower average principal balances of capital equipment leases.

Liquidity and Capital Resources

Cash Flows

The following table provides information regarding our cash position, cash flows and capital expenditures for the years ended December 31, 2012, 2011 and 2010.

	Year Ended December 31,		
	2012	2011	2010
	(dollars in millions)		
Cash, cash equivalents and marketable securities	$ 100.6	$ 39.7	$ 51.0
Working capital	77.9	25.1	34.8
Cash flows (used in) provided by:			
Operating activities	(54.1)	(47.3)	(38.2)
Investing activities	(9.9)	9.3	(19.8)
Financing activities	115.5	36.7	45.2
Capital expenditures (included in investing activities)	(0.5)	(0.7)	(0.1)

Our operating activities used cash of $54.1 million, $47.3 million and $38.2 million in 2012, 2011 and 2010, respectively. The use of cash in these periods principally resulted from our losses from operations, as adjusted for non-cash charges for depreciation and stock-based compensation, and changes in our working capital accounts.

In 2012, our investing activities used cash of $9.9 million, including the purchases of marketable securities in the amount of $50.0 million and purchases of property and equipment in the amount of $0.5 million, offset by maturities of marketable securities in our investment portfolio in the amount of $40.6 million. In 2011, our investing activities provided cash of $9.3 million, including maturities of marketable securities in our investment portfolio in the amount of $60.7 million, offset by the purchases of marketable securities in the amount of $50.7 million and purchases of property and equipment in the amount of $0.7 million. In 2010, our investing activities used cash of $19.8 million, including purchases of marketable securities in the amount of $36.9 million and purchases of property and equipment in the amount of $0.1 million, offset by $17.2 million in maturities of marketable securities in our investment portfolio.

Our financing activities provided cash of $115.5 million, $36.7 million, $45.2 million in 2012, 2011 and 2010, respectively. In 2012, we raised approximately $119.7 million in net cash proceeds, including $33.0 million in net proceeds from the sale of 8,050,000 shares of our common stock in a public offering in January 2012 and February 2012, $25.8 million in net proceeds from the sale of 3,976,702 shares of our common stock in a registered direct offering in July 2012, $59.8 million in net proceeds from the sale of 7,000,000 shares of our common stock in a registered direct offering in December 2012 and $1.1 million from the exercise of common stock options. In 2011, we raised approximately $37.3 million innet cash proceeds, including $34.8 million in net proceeds from the sale of 7,191,731 shares of our common stock in an issuer-directed registered direct offering in April 2011, $2.0 million in gross proceeds from the Oxford Term Loan that was executed in March 2011 and $0.5 million from the exercise of common stock options. In 2010, we raised approximately $47.0 million in net cash proceeds, including $26.7 million in net proceeds from the sale of 6,388,889 shares of our common stock in an underwritten public offering in January 2010, $15.0 million in gross proceeds from the GECC Term Loan that was executed in September 2010, and $5.0 million in net proceeds from the direct sale of 1,440,923 shares of our common stock in November 2010 to a director, who is our largest stockholder, as well as $0.3 million from the exercise of common stock options. We repaid $4.2 million and $0.4 million in principal payments in 2012 and 2011, respectively, in connection with the GECC Term Loan and the Oxford Term Loan. In July 2012, we began making 25 equal monthly payments of principal under the GECC Term Loan. We repaid $0.2 million and $1.8 million in capital equipment leases in 2011 and 2010, respectively.

Contractual Obligations and Commitments

The following tables summarize our contractual obligations at December 31, 2012 and the effects such obligations are expected to have on our liquidity and cash flows in future periods (in millions).

Contractual Obligations (as of December 31, 2012)	Total	2013	2014 through 2015	2016 through 2017	More than 5 years
Operating and capital lease obligations(1)	$ 8.5	$ 2.2	$ 4.3	$ 2.0	$ —
GECC and Oxford Term Loans(1)	13.9	8.8	5.1	—	—
Research and development contracts(2)	44.7	30.1	14.6	—	—
Total	$ 67.1	$ 41.1	$ 24.0	$ 2.0	$ —

(1) Includes scheduled interest payments and an exit fee of $525,000 due at the time of the final payment of the outstanding principal under the GECC Term Loan.

(2) Research and development contracts principally include contracts for human clinical studies, animal studies and clinical manufacturing. In the event a study or manufacturing contract is terminated prior to the planned completion by mutual agreement between the contractor and us, the amount paid under such contracts may be less than the amounts presented.

Amounts not included in the table of Contractual Obligations and Commitments

In July 2011, we entered into a co-development agreement with one of our clinical research organizations, or CRO, for the conduct of certain company- sponsored clinical trials. Under the co-development agreement, this CRO is performing clinical research services under a reduced fee structure in exchange for a share of licensing payments and commercial revenues, if any, up to a specified maximum payment, which is defined as a multiple of the fee reduction realized.

In accordance with the termination provisions of the Roche Agreement, all rights to the CRACM licensed compounds under the agreement were returned to us. We may continue to develop CRACM alone or with another partner and may pay Roche a low single-digit royalty on any potential future sales of the licensed products.

In accordance with the termination provisions of the GSK Agreement, all rights to the elesclomol program were returned to us. We may continue to develop elesclomol alone or with another partner and may pay GSK a low single-digit royalty on any potential future sales of elesclomol.

Under various license and other agreements, we may be obligated to pay up to an aggregate of $5.5 million if specified development and commercialization milestones are met, as follows (in millions).

Milestone	Amount
Development-based milestones related to the conduct of clinical trials	$ 0.7
Development-based milestones related to regulatory submission and approval	2.8
Commercialization-based milestones	2.0
Total	$ 5.5

Registered Direct Offering

In December 2012, we entered into common stock purchase agreements with investors and certain directors, including our largest stockholder, pursuant to which we sold 7,000,000 shares of our common stock in a registered direct offering at a purchase price of $8.60 per share. These shares were sold directly to these investors and directors without a placement agent, underwriter, broker or dealer. The net proceeds to us were approximately $59.8 million after deducting estimated offering expenses payable by us.

Registered Direct Offering

In July 2012, we entered into subscription agreements with certain directors, including our largest stockholder, pursuant to which we sold 3,976,702 shares of our common stock in a registered direct offering at a purchase price of $6.49 per share. These shares were sold directly to these directors without a placement agent, underwriter, broker or dealer. The net proceeds to us were approximately $25.8 million after deducting estimated offering expenses payable by us.

Public Offering

In January and February 2012, we raised approximately $35.4 million in gross proceeds from the sale of an aggregate of 8,050,000 shares of our common stock in a public offering at a public offering price of $4.40 per share, including 7,000,000 shares in the initial closing in January 2012 and 1,050,000 shares in a second closing in February 2012 upon the full exercise of the over-allotment option granted to the underwriters. One of our directors, who is our largest stockholder, purchased 1,136,363 shares in this offering. The net offering proceeds to us were approximately $33.0 million after deducting underwriters' discounts, fees and commissions, and other offering expenses payable by us.

At-The-Market Issuance Sales Agreement with MLV

On May 2, 2012, as amended, we entered into an at-the-market issuance sales agreement, or Sales Agreement, with MLV pursuant to which we may issue and sell shares of our common stock having an aggregate offering price of up to $28 million from time to time, at our option, through MLV as our sales agent, subject to certain terms and conditions. Any shares sold will be sold pursuant to our effective shelf registration statement on Form S-3. We will pay MLV a commission of up to 3% of the gross proceeds of the sale of any shares sold through MLV. To date, no shares have been sold under the Sales Agreement.

Term Loans

General Electric Capital Corporation (GECC)

In September 2010, as amended, we entered into a $15 million loan and security agreement with GECC and one other lender, all of which was funded at the closing in September 2010, which we refer to herein as the GECC Term Loan. Interest on the borrowings under the GECC Term Loan accrues at an annual rate of 9.75%. We made interest-only payments through June 2012. In July 2012, we began making 25 equal monthly payments of principal plus accrued interest on the outstanding balance and will pay an exit fee of $525,000 upon the conclusion of the GECC Term Loan. (See Note 10 of the accompanying consolidated financial statements.)

Oxford Finance Corporation (Oxford)

In March 2011, we entered into a $2 million loan and security agreement with Oxford, all of which was funded at the closing, which we refer to herein as the Oxford Term Loan. In December 2012, we entered into a loan modification agreement with Oxford under which we may draw down up to an

additional $0.6 million in equipment financing until May 31, 2013. As of December 31, 2012, no additional financing had been used. Interest on the borrowings under the Oxford Term Loan accrues at an annual rate of 13.35%. Beginning in May 2011, we began making 36 equal monthly payments of principal plus accrued interest on the outstanding balance. (See Note 10 of the accompanying consolidated financial statements.)

Liquidity

Funding Requirements

We expect to continue to incur significant operating expenses and capital expenditures and anticipate that our expenses and losses may increase substantially in the foreseeable future as we:

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

Our funding requirements will depend on a number of factors, including:

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

- the timing, receipt, and amount of sales or royalties, if any, from ganetespib, elesclomol, STA-9584, our CRACM inhibitors, our IL-12/23 inhibitors and our other potential products.

As of December 31, 2012, we had $100.6 million in cash, cash equivalents and marketable securities, an increase of $60.9 million from $39.7 million as of December 31, 2011. This increase principally reflects the $119.7 million in net proceeds raised from the public and registered direct offerings of our common stock and exercises of common stock options in 2012, offset by our cash used in operations as discussed under "Cash Flows" above.

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

We may require significant additional funds earlier than we currently expect in order to conduct additional clinical trials and conduct additional preclinical and discovery activities. Because of the numerous risks and uncertainties associated with the development and commercialization of our drug candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated clinical trials.

To the extent our capital resources are insufficient to meet our future capital requirements, we will need to finance our future cash needs through public or private equity offerings, collaboration agreements, debt financings or licensing arrangements. However, additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities or by selling convertible debt securities, further dilution to our existing stockholders may result. If we raise funds through collaboration agreements or licensing arrangements, we may be required to relinquish rights to our technologies or drug candidates, or grant licenses on terms that are not favorable to us.

If adequate funds are not available, we may be required to terminate, significantly modify or delay our research and development programs, reduce our planned commercialization efforts, or obtain funds through collaborators that may require us to relinquish rights to our technologies or drug candidates that we might otherwise seek to develop or commercialize independently. Conversely, we may elect to raise additional funds even before we need them if the conditions for raising capital are favorable. We currently have an effective shelf registration statement on Form S-3, under which we currently have up to $28.6 million in securities available for issuance, including up to $28 million in shares of common stock that we have reserved and that may be offered and sold under the at-the-market issuance sales agreement with MLV. We plan to file a new shelf registration statement on Form S-3 in March 2013 to register up to $300 million of our securities for future issuance.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements or relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities.

Tax Loss Carryforwards

For tax years through 2012, we performed analyses to determine if there were changes in ownership, as defined by Section 382 of the Internal Revenue Code that would limit our ability to utilize certain net operating loss and tax credit carryforwards. We determined that we experienced a change in ownership, as defined by Section 382, in connection with the acquisition of Principia Associates, Inc. on September 20, 2002, but did not experience a change in ownership upon the effectiveness of our IPO or any other equity offerings to date. As a result, the utilization of our federal tax net operating loss carryforwards generated prior to the ownership change is limited. As of December 31, 2012 we have net operating loss carryforwards for U.S. federal tax purposes of approximately $400.2 million, after taking into consideration net operating losses expected to expire unused as a result of this limitation, and the remainder will expire in varying amounts through 2032 unless utilized. In addition, as of December 31, 2012, we have state net operating loss carryforwards of approximately $157.8 million, which will expire through 2032 unless utilized. The utilization of these net operating loss carryforwards may be further limited as we experience future ownership changes as defined in Section 382 of the Internal Revenue Code.

Certain Factors That May Affect Future Results of Operations

The Securities and Exchange Commission encourages companies to disclose forward- looking information so that investors can better understand a company's future prospects and make informed investment decisions. This Annual Report on Form 10-K contains such "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995.

Words such as "may," "anticipate," "estimate," "expects," "projects," "intends," "plans," "believes" and words and terms of similar substance used in connection with any discussion of future operating or financial performance, identify forward-looking statements. All forward-looking statements are management's present expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those described in the forward-looking statements. These risks include, but are not limited to those set forth under the heading "Risk Factors" contained in Item 1A of this Annual Report on Form 10-K.

In light of these assumptions, risks and uncertainties, the results and events discussed in the forward-looking statements contained in this Annual Report on Form 10-K or in any document incorporated by reference might not occur. Stockholders are cautioned not to place undue reliance on the forward-looking statements, which speak only as of the date of this Annual Report on Form 10-K. 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 Synta or to any person acting on its behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

Item 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Sensitivity. As of December 31, 2012, we had cash, cash equivalents and marketable securities of $100.6 million consisting of cash deposited in a highly rated financial institution in the United States and in a short-term U.S. Treasury money market fund, as well as high-grade corporate bonds and commercial paper. The primary objective of our investment activities is to preserve our capital for the purpose of funding operations and we do not enter into investments for trading or

speculative purposes. We believe that we did not have material exposure to high-risk investments such as mortgage-backed securities, auction rate securities or other special investment vehicles within our money-market fund investments. We believe that we do not have any material exposure to changes in fair value as a result of changes in interest rates. Declines in interest rates, however, would reduce future investment income.

Capital Market Risk. We currently have no product revenues and depend on funds raised through other sources. One possible source of funding is through further equity offerings. Our ability to raise funds in this manner depends upon capital market forces affecting our stock price.

Item 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The information required by this Item 8 is included at the end of this Annual Report on Form 10-K beginning on page F-1.

Item 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

Not applicable.

Item 9A. CONTROLS AND PROCEDURES

1. Disclosure Controls and Procedures

Our principal executive officer and principal financial officer evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended) as of the end of the period covered by this Annual Report on Form 10-K. Based on the evaluation of our disclosure controls and procedures as of December 31, 2012, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective to ensure that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms, and is accumulated and communicated to our management, including our principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure.

2. Internal Control Over Financial Reporting

(a) Management's Annual Report on Internal Control Over Financial Reporting

Management's Annual Report On Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the Securities Exchange Act of 1934, as amended. Our internal control system was designed to provide reasonable assurance to our management and board of directors regarding the preparation and fair presentation of published financial statements. Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2012. In making this assessment, it used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control—Integrated

Framework. Based on our assessment we believe that, as of December 31, 2012, our internal control over financial reporting is effective at a reasonable assurance level based on those criteria.

Our independent registered public accounting firm has issued its report on the effectiveness of our internal control over financial reporting. This report appears below.

(b) Attestation Report of the Registered Public Accounting Firm

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of
Synta Pharmaceuticals Corp.

We have audited Synta Pharmaceutical Corp.'s internal control over financial reporting as of December 31, 2012, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Synta Pharmaceutical Corp.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Synta Pharmaceutical Corp.' maintained, in all material respects, effective internal control over financial reporting as of December 31, 2012, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Synta Pharmaceutical Corp. as of December 31, 2012 and 2011 and the related consolidated statements of operations, comprehensive

loss, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2012 and our report dated March 14, 2013 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 14, 2013

(c) Changes in Internal Controls Over Financial Reporting

There were no changes in our internal control over financial reporting, identified in connection with the evaluation of such internal control that occurred during the fourth quarter of our last fiscal year, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. OTHER INFORMATION

Not applicable.

PART III

Item 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Management and Corporate Governance," "Section 16(a) Beneficial Ownership Reporting Compliance" and "Code of Conduct and Ethics" in our Proxy Statement for the 2013 Annual Meeting of Stockholders.

We have adopted a code of conduct and ethics that applies to all of our directors, officers and employees. This code is publicly available on our website at *www.syntapharma.com.* Amendments to the code of conduct and ethics or any grant of a waiver from a provision of the code requiring disclosure under applicable Securities and Exchange Commission and The NASDAQ Stock Market rules will be disclosed in a Current Report on Form 8-K.

Item 11. EXECUTIVE COMPENSATION

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Compensation Discussion and Analysis," "Executive Officer and Director Compensation," "Management and Corporate Governance—Committees of the Board of Directors and Meetings" and "Compensation Committee Report" in our Proxy Statement for the 2013 Annual Meeting of Stockholders.

Item 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" in our Proxy Statement for the 2013 Annual Meeting of Stockholders.

Item 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The response to this item is incorporated by reference from the discussion responsive thereto under the captions "Certain Relationships and Related Person Transactions," "Management and Corporate Governance—The Board of Directors" and "Management and Corporate Governance—Director Independence" in our Proxy Statement for the 2013 Annual Meeting of Stockholders.

Item 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The response to this item is incorporated by reference from the discussion responsive thereto under the proposal captioned "Independent Registered Public Accounting Firm" in our Proxy Statement for the 2013 Annual Meeting of Stockholders.

PART IV

Item 15. **EXHIBITS AND FINANCIAL STATEMENT SCHEDULES**

Item 15(a) The following documents are filed as part of this Annual Report on Form 10-K:

Item 15(a)(1) and (2) The Consolidated Financial Statements beginning on page F-1 are filed as part of this Annual Report on Form 10-K. Other financial statement schedules have not been included because they are not applicable or the information is included in the financial statements or notes thereto.

Item 15(a)(3) Exhibits

The following is a list of exhibits filed as part of this Annual Report on Form 10-K.

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
3.1	Restated Certificate of Incorporation of the Registrant.		S-1/A (Exhibit 3.2)	1/23/07	333-138894
3.2	Restated Bylaws of the Registrant.		S-1/A (Exhibit 3.4)	1/23/07	333-138894
4.1	Form of Common Stock Certificate.		S-1/A (Exhibit 4.1)	2/5/07	333-138894
4.2.1	Amended and Restated Investor Rights Agreement, dated December 13, 2002, by and among the Registrant and certain stockholders of the Registrant.		S-1/A (Exhibit 4.2.1)	12/1/06	333-138894
4.2.2	First Amendment, dated January 11, 2005, to the Amended and Restated Investor Rights Agreement, dated December 13, 2002, by and among the Registrant and certain stockholders of the Registrant.		S-1/A (Exhibit 4.2.2)	12/1/06	333-138894
4.2.3	Second Amendment, dated January 31, 2007, to the Amended and Restated Investor Rights Agreement, dated December 13, 2002, by and among the Registrant and certain stockholders of the Registrant.		S-1/A (Exhibit 4.2.3)	2/5/07	333-138894
4.2.4	Third Amendment, dated		8-K	12/1/11	001-33277

November 30, 2011, to the Amended and Restated Investor Rights Agreement, dated December 13, 2002, by and among the Registrant and certain stockholders of the Registrant.	(Exhibit 10.1)

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
Lease Agreements					
10.1	Duffy Hartwell Limited Partnership Commercial Lease, dated November 4, 1996, by and between Duffy Hartwell Limited Partnership and Shionogi BioResearch Corp., as amended by First Amendment to Commercial Lease, dated August 30, 2006.		S-1/A (Exhibit 10.5)	12/1/06	333-138894
10.1.1	Second Amendment, dated May 27, 2008, to Commercial Lease by and between Duffy Hartwell LLC, as successor in interest to Duffy Hartwell Limited Partnership, and the Registrant, as successor in interest to Shionogi BioResearch Corp., dated November 4, 1996, as amended.		10-Q (Exhibit 10.1)	8/7/08	001-33277
10.1.2	Third Amendment, dated April 19, 2011, to Commercial Lease by and between Duffy Hartwell LLC, as successor in interest to Duffy Hartwell Limited Partnership, and the Registrant, as successor in interest to Shionogi BioResearch Corp., dated November 4, 1996, as amended.		8-K (Exhibit 10.1)	4/22/11	001-33277
10.2	Lease Agreement, dated as of June 9, 2011, by and between the Registrant and 125 Hartwell Trust.		10-Q (Exhibit 10.3)	8/4/11	001-33277

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
10.3	Pinnacle Properties Management, Inc. Standard Form Commercial Lease, dated May 31, 1999, by and between 6-8 Preston Court, L.L.C. and Asiana Pharmaceuticals Corporation, as amended by Amendment to Lease #1, dated July 31, 2000, Amendment to Lease #2, dated November 26, 2001, and Amendment to Lease #3, dated December 2003, and as assigned to the Registrant by Assignment and Assumption of Lease and Landlord's Consent, dated May 25, 2005, and Subordination, Non-Disturbance and Attornment Agreement, dated May 25, 2005.		S-1/A (Exhibit 10.8)	12/1/06	333-138894
10.4	Lease Agreement, dated December 14, 2006, by and between ARE-MA Region No. 24, LLC and the Registrant.		S-1/A (Exhibit 10.27)	1/4/07	333-138894
10.4.1	First Amendment, dated as of June 23, 2011, to Lease Agreement, dated December 14, 2006, by and between ARE-MA Region No. 24, LLC and the Registrant.		10-Q (Exhibit 10.4)	8/4/11	001-33277
Credit Facilities, Loan and Equity Agreements					
10.5	Common Stock Purchase Agreement, dated October 4, 2010, by and between the Registrant and Azimuth Opportunity Ltd.		8-K (Exhibit 10.1)	10/5/10	001-33277
10.5.1	Amendment No. 1, dated August 19, 2011, to Common Stock Purchase Agreement, dated October 4, 2010, by and between Synta Pharmaceuticals Corp. and Azimuth Opportunity Ltd.		8-K (Exhibit 10.1)	8/19/11	001-33277

10.6	Loan and Security Agreement, dated as of September 30, 2010, by and among the Registrant, Synta Securities Corp., General Electric Capital Corporation, and MidCap Funding III, LLC.	8-K (Exhibit 10.1.1)	10/5/10	001-33277

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
10.6.1	First Amendment, dated as of November 9, 2010, to Loan and Security Agreement, dated as of September 30, 2010, by and among the Registrant, Synta Securities Corp., General Electric Capital Corporation, and MidCap Funding III, LLC.		10-K (Exhibit 10.11)	3/11/11	001-33277
10.6.2	Second Amendment, dated as of March 3, 2011, to Loan and Security Agreement, dated as of September 30, 2010, as amended, by and among the Registrant, Synta Securities Corp., General Electric Capital Corporation, and MidCap Funding III, LLC.		10-Q (Exhibit 10.2)	5/5/11	001-33277
10.6.3	Third Amendment, dated as of July 1, 2011, to Loan and Security Agreement, dated as of September 30, 2010, as amended, by and among the Registrant, Synta Securities Corp., General Electric Capital Corporation, and MidCap Funding III, LLC.		10-Q (Exhibit 10.5)	8/4/11	001-33277
10.6.4	Fourth Amendment, dated as of January 23, 2012, to Loan and Security Agreement, dated as of September 30, 2010, as amended, by and among the Registrant, Synta Securities Corp., General Electric Capital Corporation, and MidCap Funding III, LLC.		10-K (Exhibit 10.6.4)	2/22/11	001-33277
10.6.5	Fifth Amendment, dated as of July 30, 2012, to Loan and Security Agreement, dated as of September 30, 2010, as amended, by and among the Registrant, Synta Securities Corp., General Electric Capital Corporation, and MidCap Funding III, LLC.		10-Q (Exhibit 10.2)	8/2/12	001-33277

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
10.6.6	Sixth Amendment, dated as of December 6, 2012, to Loan and Security Agreement, dated as of September 30, 2010, as amended, by and among the Registrant, Synta Securities Corp., General Electric Capital Corporation, and MidCap Funding III, LLC.	X			
10.6.7	Seventh Amendment, dated as of December 14, 2012, to Loan and Security Agreement, dated as of September 30, 2010, as amended, by and among Synta Pharmaceuticals Corp., Synta Securities Corp., General Electric Capital Corporation, and MidCap Funding III, LLC.		8-K (Exhibit 10.1)	12/20/12	001-33277
10.7	Promissory Note issued by the Registrant to General Electric Capital Corporation.		8-K (Exhibit 10.1.2)	10/5/10	001-33277
10.8	Promissory Note issued by the Registrant to MidCap Funding III, LLC.		8-K (Exhibit 10.1.3)	10/5/10	001-33277
10.9	Guaranty, dated as of September 30, 2010, by and among Synta Securities Corp. and General Electric Capital Corporation.		8-K (Exhibit 10.1.4)	10/5/10	001-33277
10.10	Pledge Agreement, dated as of September 30, 2010, by and among the Registrant, Synta Securities Corp., and General Electric Capital Corporation.		8-K (Exhibit 10.1.5)	10/5/10	001-33277
10.11	At the Market Issuance Sales Agreement, dated May 2, 2012, by and between the Registrant and MLV & Co. LLC.		10-Q (Exhibit 10.1)	5/3/12	001-33277
10.11.1	First Amendment, dated December 12, 2012, to the At the Market Issuance Sales Agreement, dated May 2, 2012, by and between the		8-K (Exhibit 10.2)	12/13/12	001-33277

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
10.12	Form of Subscription Agreement, dated July 25, 2012, by and between the Registrant and each of the Purchasers participating in the Registrant's July Registered Direct Offering.		8-K (Exhibit 10.1)	7/26/12	001-33277
10.13	Form of Common Stock Purchase Agreement, dated December 12, 2012, by and each of the Purchasers participating in the Registrant's December Registered Direct Offering.		8-K (Exhibit 10.1)	12/13/12	001-33277
	Agreements with Respect to Collaborations, Licenses, Research and Development				
†10.14	Collaborative Development, Commercialization and License Agreement, dated October 8, 2007, by and between the Registrant and GlaxoSmithKline.		10-K (Exhibit 10.24)	3/20/08	001-33277
†10.14.1	Amendment No. 1, dated June 27, 2008, to Collaborative Development, Commercialization and License Agreement, dated October 8, 2007, by and between the Registrant and GlaxoSmithKline.		10-Q (Exhibit 10.4)	8/7/08	001-33277
†10.15	Collaboration and License Agreement, dated December 23, 2008, by and between the Registrant and F. Hoffmann-La Roche Ltd, and its affiliate, Hoffman-La Roche Inc.		10-K/A (Exhibit 10.27)	11/10/09	001-33277
†10.15.1	Amendment, dated February 5, 2010, to Collaboration and License Agreement, dated December 23, 2008, by and between the Registrant and F. Hoffmann-La Roche Ltd, and its affiliate, Hoffman-La Roche Inc.		10-Q (Exhibit 10.1)	5/4/10	001-33277

†10.15.2	Second Amendment, executed February 3, 2011, to Collaboration and License Agreement, dated December 23, 2008, as amended, by and between the Registrant and F. Hoffmann-La Roche Ltd, and its affiliate, Hoffman-La Roche Inc.	10-Q (Exhibit 10.1)	5/5/11	001-33277

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
†10.15.3	Third Amendment, executed July 15, 2011, to Collaboration and License Agreement, dated December 23, 2008, as amended, by and between Synta Pharmaceuticals Corp. and F. Hoffmann-La Roche Ltd, and its affiliate, Hoffmann-La Roche Inc.		8-K (Exhibit 10.1)	7/21/11	001-33277
Equity Compensation Plans					
*10.16	2001 Stock Plan.		S-1/A (Exhibit 10.1)	12/1/06	333-138894
*10.17	Amended and Restated 2006 Stock Plan.		8-K (Exhibit 10.1)	6/21/10	001-33277
*10.18	Form of incentive stock option agreement under 2006 Stock Plan.		S-1/A (Exhibit 10.2(a))	1/23/07	333-138894
*10.19	Form of nonqualified stock option agreement under 2006 Stock Plan.		S-1/A (Exhibit 10.2(b))	1/23/07	333-138894
*10.20	Form of restricted stock agreement under 2006 Stock Plan.		S-1/A (Exhibit 10.2(c))	1/23/07	333-138894
*10.21	Form of nonqualified stock option agreement for directors under 2006 Stock Plan.		S-1/A (Exhibit 10.2(d))	1/23/07	333-138894
*10.22	Form of restricted stock agreement for directors under 2006 Stock Plan.		S-1/A (Exhibit 10.2(e))	1/23/07	333-138894
Agreements with Executive Officers and Directors					
*10.23	Amended and Restated Director Compensation Policy, effective March 6, 2012.		10-Q (Exhibit 10.2)	5/3/12	001-33277
*10.24	Non-Qualified Stock Option Agreement, dated February 27, 2008, by and between the Registrant and Keith R. Gollust.		10-K (Exhibit 10.4)	3/20/08	001-33277

*10.25	Letter Agreement, dated April 18, 2005, by and between the Registrant and Safi R. Bahcall, Ph.D.	S-1/A (Exhibit 10.13)	12/1/06	333-138894
*10.26	Letter Agreement, dated October 12, 2002, by and between the Registrant and Dr. Keizo Koya.	S-1/A (Exhibit 10.14)	12/1/06	333-138894
*10.27	Letter Agreement, dated February 19, 2004, by and between the Registrant and Keith Ehrlich.	S-1/A (Exhibit 10.17)	12/1/06	333-138894

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
*10.28	Letter Agreement, dated January 14, 2003, by and between the Registrant and Wendy E. Rieder.		S-1/A (Exhibit 10.18)	12/1/06	333-138894
*10.29	Letter Agreement, dated December 9, 2008, by and between the Registrant and Vojo Vukovic.		10-K (Exhibit 10.29)	3/11/10	001-33277
*10.30	Letter Agreement, dated November 19, 2010, by and between the Registrant and Amar Singh.		10-K (Exhibit 10.36)	3/11/11	001-33277
*10.31	Form of Severance and Change in Control Agreement between the Registrant and each of Keizo Koya, Amar Singh and Vojo Vukovic.		10-K (Exhibit 10.30)	3/11/10	001-33277
*10.32	Form of Severance and Change in Control Agreement between the Registrant and each of Keith S. Ehrlich and Wendy E. Rieder.		10-K (Exhibit 10.31)	3/11/10	001-33277
*10.33	Retention Award from the Registrant to Keith S. Ehrlich, dated April 14, 2009.		10-Q (Exhibit 10.3)	8/4/09	001-33277
*10.34	Agreement and Release, dated January 14, 2005, by and between the Registrant and Lan Bo Chen, Ph.D.		S-1/A (Exhibit 10.22)	12/1/06	333-138894
*10.35	Consulting Agreement, dated April 18, 2005, by and between the Registrant and Lan Bo Chen, Ph.D.		S-1/A (Exhibit 10.23)	12/1/06	333-138894
*10.35.1	Amendment to Consulting Agreement, dated March 23, 2007, by and between the Registrant and Lan Bo Chen, Ph.D.		10-K (Exhibit 10.19.1)	3/20/08	001-33277
10.36	Form of Indemnification Agreement between the Registrant and its directors and executive officers.		S-1/A (Exhibit 10.26)	12/1/06	333-138894

10.37	Subscription Agreement, dated November 10, 2010, by and between the Registrant and Bruce Kovner.	8-K (Exhibit 10.1)	11/12/10	001-33277
10.38	Form of Common Stock Purchase Agreement, dated April 14, 2011, by and among the Registrant and each of the Investors participating in the Registrant's Registered Direct Common Stock Offering.	8-K (Exhibit 10.1)	4/15/11	001-33277

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
21.1	List of Subsidiaries.		10-K (Exhibit 21.1)	3/28/07	001-33277
23.1	Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm.	X			
31.1	Certification of Principal Executive Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of Principal Accounting and Financial Officer under Section 302 of the Sarbanes-Oxley Act of 2002.	X			
32.1	Certification of the Principal Executive Officer and the Principal Accounting and Financial Officer under Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101**	The following materials from Synta Pharmaceuticals Corp.'s Annual Report on Form 10-K for the year ended December 31, 2012, formatted in XBRL (eXtensible Business Reporting Language): (i) the Consolidated Balance Sheets, (ii) the Consolidated Statements of Operations, (iii) the Consolidated Statements of Stockholders' Equity and Comprehensive Loss, (iv) the Consolidated Statements of Cash Flows, and (v) Notes to Consolidated Financial Statements.	X			

* Management contract, compensatory plan or arrangement.

† Confidential portions of these documents have been filed separately with the Securities and Exchange Commission pursuant to a request for confidential treatment.

** Users of the XBRL data are advised pursuant to Rule 406T of Regulation S-T that this interactive data file is deemed not filed or

part of a registration statement or prospectus for purposes of sections 11 or 12 of the Securities Act of 1933, is deemed not filed for purposes of section 18 of the Securities Exchange Act of 1934, and otherwise is not subject to liability under these sections.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

SYNTA PHARMACEUTICALS CORP.

Date: March 14, 2013 By: /s/ SAFI R. BAHCALL

Safi R. Bahcall, Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities indicated below and on the dates indicated.

Signatures	Title	Date
/s/ SAFI R. BAHCALL Safi R. Bahcall, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	March 14, 2013
/s/ KEITH S. EHRLICH Keith S. Ehrlich, C.P.A.	Vice President, Finance and Administration, Chief Financial Officer (principal accounting and financial officer)	March 14, 2013
/s/ KEITH R. GOLLUST Keith R. Gollust	Chairman of the Board	March 14, 2013
/s/ BRUCE KOVNER Bruce Kovner	Director	March 14, 2013
/s/ DONALD W. KUFE Donald W. Kufe, M.D.	Director	March 14, 2013
/s/ WILLIAM REARDON William Reardon, C.P.A.	Director	March 14, 2013
/s/ ROBERT N. WILSON Robert N. Wilson	Director	March 14, 2013

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

SYNTA PHARMACEUTICALS CORP.

Years ended December 31, 2012, 2011, and 2010

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Synta Pharmaceuticals Corp.

We have audited the accompanying consolidated balance sheets of Synta Pharmaceuticals Corp. (the "Company") as of December 31, 2012 and 2011, and the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2012. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Synta Pharmaceuticals Corp. at December 31, 2012 and 2011, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2012, in conformity with U.S. generally accepted accounting principles.

We have also audited, in accordance with standards of the Public Company Accounting Oversight Board (United States), the Company's internal control over financial reporting as of December 31, 2012, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 14, 2013, expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 14, 2013

SYNTA PHARMACEUTICALS CORP.

Consolidated Balance Sheets

(in thousands, except share and per share amounts)

	December 31, 2012	December 31, 2011
Assets		
Current assets:		
Cash and cash equivalents	$ 81,512	$ 30,075
Marketable securities	19,087	9,650
Prepaid expenses and other current assets	786	561
Total current assets	101,385	40,286
Property and equipment, net	1,174	1,407
Other assets	458	631
Total assets	$ 103,017	$ 42,324
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 5,661	$ 3,467
Accrued contract research costs	4,761	2,841
Other accrued liabilities	5,127	4,594
Current portion of capital lease obligations	13	12
Current portion of term loans	7,924	4,234
Total current liabilities	23,486	15,148
Long-term liabilities:		
Capital lease obligations, net of current portion	1	14
Term loans, net of current portion	4,464	12,388
Total long-term liabilities	4,465	12,402
Total liabilities	27,951	27,550
Commitments and contingencies (Note 10) Stockholders' equity:		
Preferred stock, par value $0.0001 per share Authorized: 5,000,000 shares at December 31, 2012 and 2011; no shares issued and outstanding at December 31, 2012 and 2011	—	—
Common stock, par value $0.0001 per share Authorized: 100,000,000 shares at December 31, 2012 and 2011; 68,930,082 and 49,539,808 shares issued and outstanding at December 31, 2012 and 2011, respectively	7	5
Additional paid-in-capital	536,277	413,196
Accumulated other comprehensive income	2	3
Accumulated deficit	(461,220)	(398,430)
Total stockholders' equity	75,066	14,774
Total liabilities and stockholders' equity	$ 103,017	$ 42,324

See accompanying notes to consolidated financial statements.

SYNTA PHARMACEUTICALS CORP.

Consolidated Statements of Operations

(in thousands, except share and per share amounts)

	Years Ended December 31,		
	2012	2011	2010
Revenues:			
Collaboration revenues:			
License and milestone revenue	$ —	$ 6,731	$ 4,572
Cost sharing reimbursements, net	—	—	9,253
Total collaboration revenues	—	6,731	13,825
Grant revenue	147	853	978
Total revenues	147	7,584	14,803
Operating expenses:			
Research and development	49,412	41,464	40,252
General and administrative	11,676	11,552	11,449
Total operating expenses	61,088	53,016	51,701
Loss from operations	(60,941)	(45,432)	(36,898)
Interest expense, net	(1,849)	(1,948)	(569)
Net loss	$ (62,790)	$ (47,380)	$ (37,467)
Net loss per common share:			
Basic and diluted net loss per common share	$ (1.06)	$ (1.00)	$ (0.93)
Basic and diluted weighted average number of common shares outstanding	59,411,476	47,197,572	40,365,215

See accompanying notes to consolidated financial statements.

SYNTA PHARMACEUTICALS CORP.

Consolidated Statements of Comprehensive Loss

(in thousands)

	Years Ended December 31,		
	2012	2011	2010
Net loss	$ (62,790)	$ (47,380)	$ (37,467)
Other comprehensive (loss) income:			
Unrealized (loss) gain on available-for-sale securities	(1)	6	(3)
Comprehensive loss	$ (62,791)	$ (47,374)	$ (37,470)

See accompanying notes to condensed consolidated financial statements.

SYNTA PHARMACEUTICALS CORP.

Consolidated Statements of Stockholders' Equity

(in thousands, except share amounts)

	Common stock		Additional paid-in Capital	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity
	Shares	Amount				
Balance at December 31, 2009	33,978,300	$ 3	$ 338,491	$ —	$ (313,583)	$ 24,911
Issuance of common shares in equity offering, excluding to related parties, net	5,616,667	1	23,213	—	—	23,214
Issuance of common shares to related parties	2,213,145	—	8,460	—	—	8,460
Issuance of restricted common shares	180,719	—	—	—	—	—
Exercise of stock options	132,745	—	316	—	—	316
Forfeitures of restricted common shares	(31,371)	—	—	—	—	—
Compensation expense related to stock options for services	—	—	4,048	—	—	4,048
Unrealized loss on marketable securities	—	—	—	(3)	—	(3)
Net loss	—	—	—	—	(37,467)	(37,467)
Balance at December 31, 2010	42,090,205	$ 4	$ 374,528	$ (3)	$ (351,050)	$ 23,479
Issuance of common shares in equity offering, excluding to related parties, net	5,610,238	1	27,101	—	—	27,102
Issuance of common shares to related parties	1,581,493	—	7,734	—	—	7,734
Issuance of restricted common shares	70,585	—	—	—	—	—
Exercise of stock options	193,818	—	479	—	—	479
Forfeitures of restricted common shares	(6,531)	—	—	—	—	—
Compensation expense related to stock options for services	—	—	3,354	—	—	3,354
Unrealized gain						

on marketable securities	—	—	—	6	—	6
Net loss	—	—	—	—	(47,380)	(47,380)
Balance at December 31, 2011	49,539,808	$ 5	$ 413,196	$ 3	$ (398,430)	$ 14,774
Issuance of common shares in equity offering, excluding to related parties, net	11,264,102	1	65,106	—	—	65,107
Issuance of common shares to related parties	7,762,600	1	53,544	—	—	53,545
Issuance of restricted common shares	45,243	—	—	—	—	—
Exercise of stock options	322,298	—	1,141	—	—	1,141
Purchase and retirement of common shares from an officer	(3,969)	—	(32)	—	—	(32)
Compensation expense related to stock options for service	—	—	3,322	—	—	3,322
Unrealized gain on marketable securities	—	—	—	(1)	—	(1)
Net loss	—	—	—	—	(62,790)	(62,790)
Balance at December 31, 2012	68,930,082	$ 7	$ 536,277	$ 2	$ (461,220)	$ 75,066

See accompanying notes to consolidated financial statements.

SYNTA PHARMACEUTICALS CORP.

Consolidated Statements of Cash Flows

(in thousands)

	Years Ended December 31,		
	2012	2011	2010
Cash flows from operating activities:			
Net loss	$ (62,790)	$ (47,380)	$ (37,467)
Adjustments to reconcile net loss to net cash used in operating activities:			
Stock-based compensation expense	3,322	3,354	4,048
Depreciation and amortization	738	1,464	1,933
Changes in operating assets and liabilities:			
Collaboration receivable	—	116	(116)
Prepaid expenses and other current assets	(225)	(130)	(12)
Other assets	173	(265)	(8)
Accounts payable	2,194	1,542	(2,032)
Accrued contract research costs	1,920	330	412
Other accrued liabilities	533	400	(310)
Deferred collaboration revenue	—	(6,731)	(4,647)
Net cash used in operating activities	(54,135)	(47,300)	(38,199)
Cash flows from investing activities:			
Purchases of marketable securities	(50,033)	(50,726)	(36,916)
Maturities of marketable securities	40,595	60,745	17,250
Purchases of property and equipment	(505)	(690)	(136)
Net cash (used in) provided by investing activities	(9,943)	9,329	(19,802)
Cash flows from financing activities:			
Proceeds from issuances of common stock, excluding to related parties, and exercise of common stock options, net of transaction costs	66,248	27,581	23,530
Proceeds from the sale of common stock to related parties	53,545	7,734	8,460
Purchase and retirement of common stock from an officer	(32)	—	—
Proceeds from term loans	—	2,000	15,000
Payment of term loans	(4,234)	(378)	—
Payment of capital lease obligations	(12)	(201)	(1,834)
Net cash provided by financing activities	115,515	36,736	45,156
Net increase (decrease) in cash and cash equivalents	51,437	(1,235)	(12,845)
Cash and cash equivalents at beginning of period	30,075	31,310	44,155
Cash and cash equivalents at end of period	$ 81,512	$ 30,075	$ 31,310
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 1,696	$ 1,911	$ 578

See accompanying notes to consolidated financial statements.

Notes to Consolidated Financial Statements

(1) Nature of Business

Synta Pharmaceuticals Corp. (the Company) was incorporated in March 2000 and commenced operations in July 2001. The Company is a biopharmaceutical company focusing 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.

The Company is subject to risks common to emerging companies in the drug development and pharmaceutical industry including, but not limited to, uncertainty of product development and commercialization, lack of marketing and sales history, dependence on key personnel, uncertainty of market acceptance of products, product liability, uncertain protection of proprietary technology, potential inability to raise additional financing and compliance with the U.S. Food and Drug Administration and other government regulations.

The Company has incurred significant operating losses since its inception and, as a result, at December 31, 2012 had an accumulated deficit of $461.2 million. Operations have been funded principally through the sale of common stock and convertible preferred stock, capital leases, non-refundable payments under the former collaboration agreements with GlaxoSmithKline (GSK) and Hoffman-La Roche (Roche), and proceeds from term loans by General Electric Capital Corporation (GECC) and Oxford Finance Corporation (Oxford) (see Note 10). At December 31, 2012, the Company had approximately $100.6 million in cash, cash equivalents and marketable securities.

Based on the Company's current operating levels, it expects its cash resources will be sufficient to fund operations into the second quarter of 2014. This estimate assumes that certain activities contemplated for 2013 will be conducted subject to the availability of sufficient financial resources. The Company expects to continue evaluating additional potential sources of funding, including partnership agreements, cost or risk-sharing agreements, equity financings or other sources.

The Company may require significant additional funds earlier than it currently expects in order to conduct additional clinical trials and continue to fund its operations. There can be no assurances, however, that additional funding will be available on favorable terms, or at all.

(2) Summary of Significant Accounting Policies

Principles of Consolidation

The consolidated financial statements include the financial statements of the Company and its wholly owned subsidiaries. All significant intercompany balances and transactions have been eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect certain reported amounts of assets and liabilities, disclosure of contingent assets and liabilities at the date of the financial statements, and the reported amounts of revenues and expenses during the reporting periods. Significant items subject to such estimates and assumptions include contract research accruals, recoverability of long-lived assets, measurement of stock-based compensation, and the periods of performance under its collaborative research and development agreements. The Company bases its estimates on historical experience and various other assumptions that management believes to be reasonable under the circumstances. Changes in estimates

(2) Summary of Significant Accounting Policies (Continued)

are recorded in the period in which they become known. Actual results could differ from those estimates.

Cash and Cash Equivalents

The Company considers all highly liquid investments with original maturities of three months or less at the date of purchase and an investment in a money market fund to be cash equivalents. Changes in cash and cash equivalents may be affected by shifts in investment portfolio maturities, as well as actual cash disbursements to fund operations.

The primary objective of the Company's investment activities is to preserve its capital for the purpose of funding operations and the Company does not enter into investments for trading or speculative purposes. The Company invests in money market funds and high-grade, short-term commercial paper, which are subject to minimal credit and market risk. The Company's cash is deposited in a highly rated financial institution in the United States. Declines in interest rates, however, would reduce future investment income.

Marketable Securities

Marketable securities consist of investments in high-grade corporate obligations, and government and government agency obligations that are classified as available-for-sale. Since these securities are available to fund current operations they are classified as current assets on the consolidated balance sheets.

The Company adjusts the cost of available-for-sale debt securities for amortization of premiums and accretion of discounts to maturity. The Company includes such amortization and accretion in interest and investment income. Realized gains and losses and declines in value, if any, that the Company judges to be other-than-temporary on available-for-sale securities are reported in interest and investment income. To determine whether an other-than-temporary impairment exists, the Company considers whether it intends to sell the debt security and, if the Company does not intend to sell the debt security, it considers available evidence to assess whether it is more likely than not that it will be required to sell the security before the recovery of its amortized cost basis. During the years ended December 31, 2012, 2011 and 2010, the Company determined that no securities were other-than-temporarily impaired.

Marketable securities are stated at fair value, including accrued interest, with their unrealized gains and losses included as a component of accumulated other comprehensive loss, which is a separate component of stockholders' equity. The fair value of these securities is based on quoted prices and observable inputs on a recurring basis. Realized gains and losses are determined on the specific identification method. During the years ended December 31, 2012, 2011 and 2010, the Company recorded no realized gains or losses on marketable securities.

Fair Value of Financial Instruments

The carrying amounts of the Company's financial instruments, which include cash equivalents, marketable securities, accounts payable and capital lease and term loan obligations, approximate their fair values. The fair value of the Company's financial instruments reflects the amounts that would be

(2) Summary of Significant Accounting Policies (Continued)

received upon sale of an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. The fair value hierarchy has the following three levels:

Level 1—quoted prices in active markets for identical assets and liabilities.

Level 2—observable inputs other than Level 1 inputs. Examples of Level 2 inputs include quoted prices in active markets for similar assets or liabilities and quoted prices for identical assets or liabilities in markets that are not active.

Level 3—unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability.

Financial assets and liabilities are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company measures the fair value of its marketable securities by taking into consideration valuations obtained from third-party pricing sources. The pricing services utilize industry standard valuation models, including both income and market based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include reported trades of and broker-dealer quotes on the same or similar securities, issuer credit spreads, benchmark securities and other observable inputs. As of December 31, 2012, the Company's financial assets valued based on Level 1 inputs consisted of cash and cash equivalents in a money market fund and its financial assets valued based on Level 2 inputs consisted of high-grade corporate bonds and commercial paper. During the year ended December 31, 2012, there were no transfers of financials assets between Levels 1 and 2. As of December 31, 2012, the Company had no financial liabilities that were recorded at fair value on the balance sheet. The fair value of the Company's term loan obligations is determined using current applicable rates for similar instruments as of the balance sheet date. The carrying value of the Company's term loan obligations approximates fair value as the Company's interest rate yield is near current market rate yields. The Company's term loan obligations are Level 3 liabilities within the fair value hierarchy.

Property and Equipment

Property, equipment and software is carried at cost and depreciated using the straight-line method over the estimated useful lives of the related assets, which range from three to five years. Leasehold improvements are amortized over the lesser of the lease term or estimated useful life. Repairs and maintenance costs are expensed as incurred.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs are comprised of costs incurred in performing research and development activities, including internal costs for salaries, benefits, facilities, research-related overhead and stock compensation, and external costs for payments to third party contract research organizations, investigative sites and consultants in connection with the Company's preclinical and clinical programs, costs associated with drug formulation and supply of drugs for clinical trials, and other external costs.

Patents

Costs to secure and defend patents are expensed as incurred and are classified as general and administrative expense in the Company's consolidated statements of operations. Patent expenses were

(2) Summary of Significant Accounting Policies (Continued)

approximately $1.8 million, $2.3 million, and $1.9 million for the years ended December 31, 2012, 2011 and 2010, respectively.

Income Taxes

The Company uses the liability method to account for income taxes. Deferred tax assets and liabilities are determined based on the expected future tax consequences of temporary differences between the Company's consolidated financial statement carrying amounts and the tax basis of assets and liabilities using enacted tax rates expected to be in effect in the years in which the differences are expected to reverse. A valuation allowance is provided to reduce the deferred tax assets to the amount that will more likely than not be realized.

As of December 31, 2012 and 2011, the Company had no items that were considered to be uncertain tax items or accrued interest or penalties related to uncertain tax positions.

The tax years 2009 through 2012 remain open to examination by the major taxing jurisdictions to which the Company is subject.

Impairment of Long-Lived Assets

The Company assesses the potential impairments of its long-lived assets whenever events or changes in circumstances indicate that an asset's carrying value may not be recoverable. If the carrying value exceeds the undiscounted future cash flows estimated to result from the use and eventual disposition of the asset, the Company writes down the asset to its estimated fair value. Management believes that no long-lived assets were impaired as of December 31, 2012 and 2011.

Revenue Recognition

Collaboration and License Agreements

The Company's principal source of revenue to date has been generated primarily through its former collaborative research and development agreements with Roche and GSK, which included upfront license payments, development milestones, reimbursement of research and development costs, and potential profit sharing payments, commercial and sales-based milestones and royalties. The application of accounting rules requires subjective analysis and requires management to make estimates and assumptions about whether deliverables within multiple-element arrangements are separable from the other aspects of the contractual arrangement into separate units of accounting and to determine the fair value to be allocated to each unit of accounting.

For multiple-element arrangements entered into or materially modified after January 1, 2011, the Company follows the provisions of ASU No. 2009-13 *Multiple-deliverable Revenue Arrangements (*ASU No. 2009-13). This standard addresses the determination of the unit(s) of accounting for multiple-element arrangements and how the arrangement's consideration should be allocated to each unit of accounting.

Pursuant to this standard, each required deliverable is evaluated to determine if it qualifies as a separate unit of accounting. For the Company this determination includes an assessment as to whether the deliverable has "stand-alone value" to the customer separate from the undelivered elements. The arrangement's consideration is then allocated to each separate unit of accounting based on the relative

(2) Summary of Significant Accounting Policies (Continued)

selling price of each deliverable. The estimated selling price of each deliverable is determined using the following hierarchy of values: (i) vendor-specific objective evidence of fair value, (ii) third-party evidence of selling price, and (iii) the Company's best estimate of the selling price (BESP). The BESP reflects the Company's best estimate of what the selling price would be if the deliverable was regularly sold by it on a stand-alone basis. The Company expects, in general, to use BESP for allocating consideration to each deliverable in future collaboration agreements. In general, the consideration allocated to each unit of accounting is then recognized as the related goods or services are delivered limited to the consideration not contingent upon future deliverables.

For multiple-element arrangements entered into prior to January 1, 2011 and not materially modified thereafter, the Company continued to apply its prior accounting policy with respect to such arrangements. Under this policy, in general, revenue from non-refundable, upfront fees related to intellectual property rights/licenses where the Company had continuing involvement was recognized ratably over the estimated period of ongoing involvement because there was no objective and reliable evidence of fair value for certain of the undelivered item to allow the delivered item to be considered a separate unit of accounting. This requirement with respect to the fair value of undelivered items was eliminated in the newly issued accounting standard. In general, the consideration with respect to the other deliverables was recognized when the goods or services were delivered.

The Company's deliverables under its former collaboration agreement with Roche, including the related rights and obligations, contractual cash flows and performance periods, are more fully described in Note 8. Certain of the deliverables were combined as a single unit of accounting.

The cash flows associated with the single unit of accounting from the research and development portions of the Company's collaborations were recognized as revenue using a time-based model. Under this model, cash flow streams were recognized as revenue over the estimated performance period. Upon achievement of milestones, as defined in the collaboration agreements, revenue was recognized to the extent the accumulated service time, if any, had occurred. The remainder was deferred and recognized as revenue ratably over the remaining estimated performance period. A change in the period of time expected to complete the deliverable was accounted for as a change in estimate on a prospective basis. Revenue was limited to amounts that were non-refundable and that the Company's collaborators were contractually obligated to pay to the Company.

Effective January 1, 2011, the Company adopted ASU No. 2009-13 which codified a method of revenue recognition that has been common practice. Under this method, contingent consideration from research and development activities that is earned upon the achievement of a substantive milestone is recognized in its entirety in the period in which the milestone is achieved. At the inception of each arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. From the effective date of the

(2) Summary of Significant Accounting Policies (Continued)

adoption of this standard, the Company did not achieve any developmental, commercial or sales-based milestones pursuant to its research and collaboration agreement with Roche. Upon the effectiveness of the termination of the collaboration agreement with Roche on February 16, 2012, as more fully described in Note 8, the Company has no ongoing research and collaboration agreements under which milestones may be achieved.

Royalty revenues are based upon a percentage of net sales. Royalties from the sales of products will be recorded on the accrual basis when results are reliably measurable, collectibility is reasonably assured and all other revenue recognition criteria are met. Commercial and sales-based milestones, which are based upon the achievement of certain agreed-upon sales thresholds, will be recognized in the period in which the respective sales threshold is achieved and collectibility is reasonably assured.

Grant Revenue

In March 2011, the Company received a grant from the Department of Defense, in the approximate amount of $1 million, for the development of STA-9584 in advanced prostate cancer. The Company conducted work on this study during the one year grant period from April 2011 through March 2012. Reimbursements were based on actual costs agreed upon in the proposal (salary, fringe benefits, overhead, and direct costs such as materials and subcontractors). The Company recognized $147,000 and $853,000 of grant revenue under this grant in the years ended December 31, 2012 and 2011, respectively.

In November 2010, the Company was awarded approximately $1.0 million in grants under the Patient Protection and Affordable Care Act. The Company recognized approximately $1.0 million of grant revenue under these grants in the year ended December 31, 2010.

Stock-Based Compensation

The Company recognizes stock-based compensation expense based on the fair value of stock options granted to employees, officers and directors. The Company uses the Black-Scholes option pricing model as it is the most appropriate valuation method for its option grants. The Black-Scholes model requires inputs for risk-free interest rate, dividend yield, volatility and expected lives of the options. Expected volatility was principally based upon the weighted average historical volatility data of the Company's common stock and the historical volatility data from several guideline public biotechnology companies similar in size and value to the Company that also have stock compensation plans with similar terms. The Company estimates the forfeiture rate based on historical data. Based on an analysis of historical forfeitures, the Company has applied a forfeiture rate of 10% to all options that vest upon completion of the first year of service following the date of grant. The analysis is re-evaluated at least annually and the forfeiture rate is adjusted as necessary. The risk-free rate for periods within the expected life of the option is based on the U.S. Treasury yield curve in effect at the time of the grant. The expected lives for options granted represent the period of time that options granted are expected to be outstanding. The Company uses the simplified method for determining the expected lives of options.

For awards with graded vesting, the Company allocates compensation costs on a straight-line basis over the requisite service period. The Company amortizes the fair value of each option over each option's service period, which is generally the vesting period.

(2) Summary of Significant Accounting Policies (Continued)

Certain of the employee stock options granted by the Company are structured to qualify as incentive stock options (ISOs). Under current tax regulations, the Company does not receive a tax deduction for the issuance, exercise or disposition of ISOs if the employee meets certain holding requirements. If the employee does not meet the holding requirements, a disqualifying disposition occurs, at which time the Company may receive a tax deduction. The Company does not record tax benefits related to ISOs unless and until a disqualifying disposition is reported. In the event of a disqualifying disposition, the entire tax benefit is recorded as a reduction of income tax expense. The Company has not recognized any income tax benefit for the share-based compensation arrangement due to the fact that the Company does not believe it is more likely than not it will recognize any deferred tax assets from such compensation cost recognized in the current period.

Comprehensive Loss

Comprehensive loss is defined as the change in equity of a business enterprise during a period from transactions, and other events and circumstances from non-owner sources. Changes in unrealized gains and losses on marketable securities represent the only difference between the Company's net loss and comprehensive loss.

In the first quarter of 2012, the Company adopted ASU No. 2011-05, *Comprehensive Income (Topic 220): Presentation of Comprehensive Income* (ASU No. 2011-05). ASU No. 2011-05 requires companies to present the components of net income and other comprehensive income either as one continuous statement or as two consecutive statements, eliminating the option to present components of other comprehensive income as part of the statement of changes in stockholders' equity. This update does not change the items which must be reported in other comprehensive income, how such items are measured or when they must be reclassified to net income. Upon adoption, the Company elected to present comprehensive income in two separate but consecutive statements as part of the consolidated financial statements included in this Annual Report on Form 10-K.

Segment Reporting

Operating segments are determined based on the way management organizes its business for making operating decisions and assessing performance. The Company has only one operating segment, the discovery, development and commercialization of drug products.

Basic and Diluted Loss Per Common Share

Basic net loss per share is computed using the weighted average number of common shares outstanding during the period, excluding restricted stock that has been issued but is not yet vested. Diluted net loss per common share is computed using the weighted average number of common shares outstanding and the weighted average dilutive potential common shares outstanding using the treasury stock method. However, for the years ended December 31, 2012, 2011 and 2010, diluted net loss per share is the same as basic net loss per share as the inclusion of weighted average shares of unvested restricted common stock and common stock issuable upon the exercise of stock options would be anti-dilutive.

(2) Summary of Significant Accounting Policies (Continued)

The following table summarizes outstanding securities not included in the computation of diluted net loss per common share as their inclusion would be anti-dilutive:

	Years Ended December 31,		
	2012	2011	2010
Common stock options	5,521,584	5,821,073	5,326,979
Unvested restricted stock	35,122	82,450	140,613

(3) Cash, Cash Equivalents and Marketable Securities

A summary of cash, cash equivalents and available-for-sale marketable securities held by the Company as of December 31, 2012 and 2011 was as follows (see Note 2):

	December 31, 2012			
	Cost	Unrealized gains	Unrealized losses	Fair value
	(in thousands)			
Cash and cash equivalents:				
Cash and money market funds (Level 1)	$ 81,512	$ —	$ —	$ 81,512
Marketable securities:				
Corporate debt securities due within 1 year of date of purchase (Level 2)	19,085	3	(1)	19,087
Total cash, cash equivalents and marketable securities	$ 100,597	$ 3	$ (1)	$ 100,599

	December 31, 2011			
	Cost	Unrealized gains	Unrealized losses	Fair value
	(in thousands)			
Cash and cash equivalents:				
Cash and money market funds (Level 1)	$ 25,326	$ —	$ —	$ 25,326
Government-sponsored entities and corporate debt securities due within 3 months of date of purchase (Level 2)	4,749	—	—	4,749
Total cash and cash equivalents	$ 30,075	$ —	$ —	$ 30,075
Marketable securities:				
Corporate debt securities due within 1 year of date of purchase (Level 2)	9,647	3	—	9,650
Total cash, cash equivalents and marketable securities	$ 39,722	$ 3	$ —	$ 39,725

(4) Property and Equipment

Property and equipment consist of the following:

	December 31, 2012	December 31, 2011
	(in thousands)	
Laboratory equipment	$ 12,531	$ 12,468
Leasehold improvements	4,939	4,847
Computers and software	2,630	2,315
Furniture and fixtures	1,170	1,135
	21,270	20,765
Less accumulated depreciation and amortization	(20,096)	(19,358)
	$ 1,174	$ 1,407

Depreciation and amortization expenses of property and equipment, including equipment purchased under capital leases, were approximately $0.7 million, $1.5 million and $1.9 million for the years ended December 31, 2012, 2011 and 2010, respectively.

The net book value and accumulated amortization of equipment under capital lease was approximately $1,000 and $57,000, respectively, at December 31, 2012, and $16,000 and $43,000, respectively, at December 31, 2011.

(5) Stockholders' Equity

Common Stock

Each common stockholder is entitled to one vote for each share of stock held. The common stock will vote together with all other classes and series of stock of the Company as a single class on all actions to be taken by the Company's stockholders. Each share of common stock is entitled to receive dividends, as and when declared by the Company's board of directors.

The Company has never declared cash dividends on its common stock and does not expect to do so in the foreseeable future.

Registered Direct Offering

In December 2012, the Company entered into common stock purchase agreements with investors and certain directors, including its largest stockholder, pursuant to which the Company sold 7,000,000 shares of its common stock in a registered direct offering at a purchase price of $8.60 per share. These shares were sold directly to these investors and directors without a placement agent, underwriter, broker or dealer. The net proceeds to the Company were approximately $59.8 million after deducting estimated offering expenses payable by the Company.

Registered Direct Offering

In July 2012, the Company entered into subscription agreements with certain directors, including its largest stockholder, pursuant to which the Company sold 3,976,702 shares of its common stock in a registered direct offering at a purchase price of $6.49 per share. These shares were sold directly to these directors without a placement agent, underwriter, broker or dealer. The net proceeds to the

(5) Stockholders' Equity (Continued)

Company were approximately $25.8 million after deducting estimated offering expenses payable by the Company.

Public Offering

In January 2012 and February 2012, the Company raised approximately $35.4 million in gross proceeds from the sale of an aggregate 8,050,000 shares of its common stock in a public offering at $4.40 per share, including 7,000,000 shares in the initial closing in January 2012 and 1,050,000 shares in a second closing in February 2012 upon the full exercise of the over-allotment option granted to the underwriters. One of the Company's directors, who is its largest stockholder, purchased 1,136,363 shares in this offering. The net offering proceeds to the Company were approximately $33.0 million after deducting underwriters' discounts, fees and commissions, and other offering expenses payable by the Company.

Equity Line of Credit

In October 2010, as amended, the Company entered into a common stock purchase agreement (Purchase Agreement) with Azimuth Opportunity Ltd. (Azimuth) pursuant to which the Company obtained an equity line of credit facility (Facility) under which it may have sold, in its sole discretion, and Azimuth was committed to purchase, subject to the terms and conditions set forth in the Purchase Agreement, up to $35 million or 8,106,329 shares of the Company's common stock, whichever was fewer, over the term of the agreement which expired on May 1, 2012. No shares were sold to Azimuth under the Facility.

At-The-Market Issuance Sales Agreement

On May 2, 2012, the Company entered into an at-the-market issuance sales agreement, as amended, (Sales Agreement) with MLV & Co. LLC (MLV), pursuant to which the Company may issue and sell shares of its common stock having an aggregate offering price of up to $28 million from time to time, at the Company's option, through MLV as its sales agent. Sales of common stock through MLV, if any, will be made by any method that is deemed an "at-the-market" offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, including by means of ordinary brokers' transactions at market prices, in block transactions or as otherwise agreed by the Company and MLV. Subject to the terms and conditions of the Sales Agreement, MLV will use commercially reasonable efforts to sell the common stock based upon the Company's instructions (including any price, time or size limits or other customary parameters or conditions the Company may impose). The Company is not obligated to make any sales of its common stock under the Sales Agreement. Any shares sold will be sold pursuant to the Company's effective shelf registration statement on Form S-3. The Company will pay MLV a commission of up to 3% of the gross proceeds. The Sales Agreement will terminate upon the earlier of the sale of all common stock subject to the Sales Agreement or termination of the Sales Agreement by the Company or MLV. To date, no shares have been sold under the Sales Agreement.

Issuer-Directed Registered Direct Offering

In April 2011, the Company raised approximately $35.2 million in gross proceeds from the sale of an aggregate of 7,191,731shares of its common stock at a purchase price of $4.89 per share, which was the closing price of the Company's common stock on the date of sale, in an issuer-directed registered

(5) Stockholders' Equity (Continued)

direct offering. The shares were sold directly to investors without a placement agent, underwriter, broker or dealer, and no warrants were issued as part of this transaction. 1,581,493 shares were sold to certain of the Company's directors and entities affiliated with these directors, and the remainder of the shares were sold to institutional investors. The proceeds to the Company were approximately $34.8 million after deducting estimated offering expenses payable by the Company.

(6) Stock-Based Compensation

The Company's 2006 Stock Plan provides for the grant of incentive stock options, nonstatutory stock options and non-vested stock to employees, officers, directors and consultants to the Company. In January 2013, the number of shares of common stock reserved for issuance under the 2006 Stock Plan was increased from 7,700,000 to 9,000,000 pursuant to an "evergreen" provision, which provides for an annual increase based on the lesser of 1,300,000 shares, 5% of the Company's then outstanding shares of common stock, or such other amount as the board of directors may determine. This increase was approved by the board of directors in December 2012. The administration of the 2006 Stock Plan is under the general supervision of the compensation committee of the board of directors. The exercise price of the stock options is determined by the compensation committee of the board of directors, provided that incentive stock options are granted at not less than fair market value of the common stock on the date of grant and expire no later than ten years from the date the option is granted. Options generally vest over four years. As of December 31, 2012, the Company had options outstanding to purchase 5,521,584 shares of its common stock, which includes options outstanding under its 2001 Stock Plan that was terminated in March 2006, and had 35,122 restricted shares of common stock outstanding. As of December 31, 2012, 1,902,341 shares were available for future issuance and were subsequently increased by an additional 1,300,000 shares in January 2013 related to the "evergreen" provision.

The following table summarizes stock option activity during the year ended December 31, 2012:

	Shares	Weighted average exercise price	Weighted average remaining contractual life (years)	Aggregate intrinsic value
Outstanding at January 1	5,821,073	$ 7.54		
Options granted	1,799,096	5.14		
Options exercised	(322,298)	3.54		
Options cancelled	(1,776,287)	9.36		
Outstanding at December 31	5,521,584	$ 6.40	6.83	$ 17,472,889
Exercisable at December 31	3,091,173	$ 7.44	5.25	$ 7,906,822

The aggregate intrinsic value of all options outstanding and exercisable represents the total pre-tax amount, net of the exercise price, which would have been received by option holders if all option holders had exercised all options with an exercise price lower than the closing stock price of $9.02 on December 31, 2012, which was the last trading day of the year. The total intrinsic value of options exercised during the years ended December 31, 2012, 2011 and 2010 was approximately $904,000, $518,000 and $278,000, respectively. The total cash received by the Company as a result of stock option exercises during 2012, 2011 and 2010 was $1.1 million, $0.5 million and $0.3 million, respectively. The weighted-average grant-date fair values of options granted during the years ended December 31, 2012, 2011 and 2010 were $4.10, $4.26 and $3.27, respectively.

(6) Stock-Based Compensation (Continued)

Non-Vested ("Restricted") Stock Awards With Service Conditions

The Company's share-based compensation plan provides for awards of restricted shares of common stock to employees, officers, directors and consultants to the Company. Restricted stock awards are subject to forfeiture if employment or service terminates during the prescribed retention period. Restricted shares vest over the service period. The total fair value of restricted stock that vested during 2012, 2011 and 2010 was $0.6 million, $0.6 million and $0.2 million, respectively.

The following table summarizes unvested restricted shares during the year ended December 31, 2012:

	Shares	Weighted average grant date fair value
Outstanding at January 1	82,450	$ 4.94
Vested	(92,571)	5.16
Granted	45,243	5.47
Outstanding at December 31	35,122	$ 5.04

Stock-Based Compensation Expense

For the years ended December 31, 2012, 2011 and 2010, the fair value of each employee stock option award was estimated on thedate of grant based on the fair value method using the Black-Scholes option pricing valuation model with the following weighted average assumptions:

	Years ended December 31,		
	2012	2011	2010
Risk-free interest rate	1.11%	2.48%	2.62%
Expected life in years	6.25 years	6.25 years	6.25 years
Volatility	101%	101%	102%
Expected dividend yield	—	—	—

(6) Stock-Based Compensation (Continued)

Stock-based compensation expense during the years ended December 31, 2012, 2011 and 2010 was as follows (in thousands):

	Years ended December 31,		
	2012	2011	2010
Stock-based compensation expense by type of award:			
Employee stock options	$ 3,082	$ 2,951	$ 3,614
Restricted stock	240	403	434
Total stock-based compensation expense	$ 3,322	$ 3,354	$ 4,048
Effect of stock-based compensation expense by line item:			
Research and development	$ 2,485	$ 2,494	$ 3,074
General and administrative	837	860	974
Total stock-based compensation expense included in net loss	$ 3,322	$ 3,354	$ 4,048

Unrecognized stock-based compensation expense as of December 31, 2012 was as follows (in thousands):

	Unrecognized stock compensation expense as of December 31, 2012	Weighted average remaining period (in years)
Employee stock options	$ 7,747	2.65
Restricted stock	172	0.62
Total	$ 7,919	2.61

7) Other Accrued Liabilities

Other accrued liabilities consist of the following:

	December 31, 2012	December 31, 2011
	(in thousands)	
Compensation and benefits	$ 3,272	$ 2,914
Professional fees	999	1,069
Other	856	611
	$ 5,127	$ 4,594

(8) License and Development Agreements

Roche

In December 2008, as amended in February 2010, February 2011 and July 2011, the Company and Roche entered into a collaborative license agreement (the Roche Agreement) to discover, develop, and commercialize small-molecule drugs targeting calcium release-activated calcium modulator (CRACM) channels. The goal of this alliance was to develop a novel category of oral, disease-modifying agents for the treatment of rheumatoid arthritis and other autoimmune diseases and inflammatory conditions. The Roche Agreement consisted of the following funding streams: an upfront license payment, reimbursements of certain research and development costs, product development milestones, sales milestones and product royalty payments.

Pursuant to the Roche Agreement, the Company received a non-refundable upfront license payment of $16 million in January 2009. Roche reimbursed all of the Company's research and certain early development costs over the two year research term that concluded on December 31, 2010. The Company received approximately $21.2 million in research and development support under the Roche Agreement.

Roche terminated the Roche Agreement effective February 16, 2012. All rights to certain products, referred to as Licensed Compounds, which were identified and studied prior to the end of the two year research term, reverted to the Company upon the effectiveness of the termination. The Company may pay Roche a low single-digit royalty on any potential future sales of licensed products. The Company did not incur any termination costs or penalties as a result of the termination of the Roche Agreement. No development milestones were achieved under the Roche Agreement.

The $16 million non-refundable upfront license payment was being recognized ratably using the time-based model over the estimated performance period through June 2012. In the fourth quarter of 2011, upon notification of Roche's election to terminate the Roche Agreement, the Company accelerated the recognition of approximately $2.1 million of remaining deferred revenue from the upfront payment because the Company had no remaining substantial performance obligations. In the years ended December 31, 2012, 2011 and 2010, the Company recognized $0, $6.7 million and $4.6 million, respectively, of license revenue under the Roche Agreement. Reimbursements of research and development costs to the Company by Roche were recorded as cost sharing revenue in the period in which the related research and development costs were incurred. In the years ended December 31, 2012, 2011 and 2010, the Company recognized $0,$0 and $9.3 million, respectively, of cost sharing revenue under the Roche Agreement.

Co-Development Agreement

In July 2011, the Company entered into a co-development agreement with a clinical research organization (CRO) for the conduct of certain company-sponsored clinical trials. Under the co-development agreement, this CRO is performing clinical research services under a reduced fee structure in exchange for a share of licensing payments and commercial revenues, if any, resulting from the product under development up to a specified maximum payment, which is defined as a multiple of the fee reduction realized.

(9) Income Taxes

Differences between the actual tax provision (benefit) and the tax provision (benefit) computed using the United States federal income tax rate is as follows:

	Years ended December 31,		
	2012	2011	2010
	(in thousands)		
Provision (benefit) at statutory rate	$ (21,349)	$ (16,109)	$ (12,739)
State taxes, net of federal benefit	(3,220)	(2,379)	(1,967)
State tax rate change	—	84	196
State net operating loss expiration	3,167	2,867	3,820
Stock-based compensation	382	373	791
Tax credits	(411)	(1,537)	(1,686)
Other	22	259	(78)
(Decrease) increase in valuation allowance	21,409	16,442	11,663
Income tax provision (benefit)	$ —	$ —	$ —

The effects of temporary differences that give rise to significant portions of deferred tax assets and deferred tax liabilities at December 31 are presented below:

	2012	2011
	(in thousands)	
Deferred tax assets:		
Federal and state net operating loss carryforwards	$ 143,988	$ 123,463
Federal and state research and experimentation credits	17,225	16,796
Depreciation and amortization	2,594	2,776
Deferred compensation	5,368	5,077
Other	1,014	667
Deferred tax assets	170,189	148,779
Less valuation allowance	(170,189)	(148,779)
Net deferred tax assets	$ —	$ —

The total valuation allowance increased by approximately $21.4 million, $16.4 million and $11.7 million in the years ended December 31, 2012, 2011 and 2010, respectively.

The Company has established valuation allowances against its deferred tax assets because management believes that, after considering all of the available objective evidence, both historical and prospective, the realization of the deferred tax assets does not meet the "more likely than not" criteria. The Company evaluates the need for a valuation allowance on a quarterly basis.

For tax years through 2012 the Company performed analyses to determine if there were changes in ownership, as defined by Section 382 of the Internal Revenue Code that would limit its ability to utilize certain net operating loss and tax credit carryforwards. The Company determined that it experienced an ownership change, as defined by Section 382, in connection with its acquisition of Principia Associates, Inc. on September 20, 2002, but did not experience a change in ownership upon the effectiveness of the Company's IPO, or any other equity offerings to date. As a result, the utilization of the Company's federal tax net operating loss carryforwards generated prior to the ownership change is

(9) Income Taxes (Continued)

limited. As of December 31, 2012, the Company has net operating loss carryforwards for U.S. federal tax purposes of approximately $400.2 million, after excluding net operating losses that have expired unused as a result of Section 382 limitations, with the remainder expiring in varying amounts through 2032 unless utilized. At December 31, 2012, the Company has state net operating loss carryforwards of approximately $157.8 million, which will expire through 2032 unless utilized. The net operating loss carryforwards include approximately $1.1 million of deductions related to the exercise of common stock options. This amount represents an excess tax benefit and has not been included in the gross deferred tax asset reflected for net operating losses.The utilization of these net operating loss carryforwards may be further limited if the Company experiences future ownership changes as defined in Section 382 of the Internal Revenue Code. Approximately $60.0 million of state net operating loss carryforwards expired in 2012.

At December 31, 2012, the Company had approximately $13.2 million and $6.1 million, respectively, in federal and state research and development credits which expire through 2031 and 2027, respectively.

The Company is currently open to examination under the statute of limitations by the Internal Revenue Service and state jurisdictions for the tax years ended 2009 through 2012. Carryforward tax attributes generated in years past may still be adjusted upon future examination if they have or will be used in a future period. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years.

The Company does not consider any of its tax positions to be uncertain and accordingly there are no tax reserves for the years ended December 31, 2012, 2011, and 2010. The Companywill recognize interest expense and penalties related to uncertain tax positions in income tax expense. The Company has not, as yet, conducted a study of its domestic research and development credit carryforwards. This study may result in an increase or decrease to the Company's research and development credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development credits, and if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. As a result, there would be no impact to the consolidated balance sheet, statement of operations and comprehensive loss or cash flows if an adjustment were required.

(10) Commitments and Contingencies

Leases

The Company leases its research and office facilities under three non-cancelable and renewable operating leases with terms expiring in the fourth quarter of 2016. These lease agreements include customary provisions for rent increases, escalations for operating costs and renewals. The Company also leases equipment under various other non-cancellable operating leases.

Term Loans

General Electric Capital Corporation

In September 2010, the Company entered into a $15 million loan and security agreement, as amended, with GECC and one other lender, all of which was funded at the closing in September 2010

(10) Commitments and Contingencies (Continued)

(the GECC Term Loan). Interest on the borrowings under the GECC Term Loan accrues at an annual rate of 9.75%.

The Company made interest-only payments through June 2012. Beginning in July 2012, the Company began making 25 equal monthly payments of principal plus accrued interest on the outstanding balance. In addition to the interest payable under the GECC Term Loan, the Company paid origination and amendment fees in the amount of $388,000 and is obligated to pay an exit fee of $525,000 at the time of the final payment of the outstanding principal.

Origination and exit fees are being amortized and accreted, respectively, to interest expense over the term of the GECC Term Loan. As of December 31, 2012, the Company had paid approximately $262,000 of legal fees and expenses in connection with the GECC Term Loan. These expenses have been deferred and, together with the origination fees, are included in other assets, and will be expensed over the term of the GECC Term Loan. In the years ended December 31, 2012, 2011 and 2010, the Company recognized approximately $321,000, $275,000 and $67,000, respectively, in interest expense in connection with these origination, exit and transaction fees and expenses. In the years ended December 31, 2012, 2011 and 2010, respectively, the Company recognized approximately $1.4 million, $1.5 million and $453,000, respectively, in interest expense related to the outstanding principal under the GECC Term Loan. No warrants were issued in connection with the GECC Term Loan. The Company may prepay the full amount of the GECC Term Loan, subject to prepayment premiums under certain circumstances.

The GECC Term Loan is secured by substantially all of the Company's assets, except its intellectual property. The Company has granted GECC a springing security interest in its intellectual property in the event the Company is not in compliance with certain cash usage covenants, as defined therein. The GECC Term Loan contains restrictive covenants, including the requirement for the Company to receive the prior written consent of GECC to enter into loans, other than up to $4.0 million of equipment financing, restrictions on the declaration or payment of dividends, restrictions on acquisitions, and customary default provisions that include material adverse events, as defined therein. The Company has determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal in current and long-term liabilities based on the timing of scheduled principal payments. In addition, at the time of the closing of the GECC Term Loan, the Company repaid approximately $787,000 of remaining principal outstanding under its existing equipment leases with GECC.

Oxford Finance Corporation

In March 2011, the Company entered into a $2 million loan and security agreement with Oxford, all of which was funded in March 2011 (the Oxford Term Loan). Interest on the borrowings under the Oxford Term Loan accrues at an annual rate of 13.35%. Beginning in May 2011, the Company began making 36 equal monthly payments of principal plus accrued interest on the outstanding balance. In December 2012, the Company entered into a loan modification agreement under which the Company may draw down up to an additional $0.6 million in equipment financing until May 31, 2013 that would be payable in 36 equal monthly payments of principal plus accrued interest on the outstanding balance. As of December 31, 2012, no additional equipment financing had been used. The Company recognized approximately $172,000 and $192,000 in the years ended December 31, 2012 and 2011,respectively, in interest expense related to the outstanding principal under the Oxford Term Loan. In addition to the

(10) Commitments and Contingencies (Continued)

interest payable under the Oxford Term Loan, the Company paid approximately $88,000 of administrative and legal fees and expenses in connection with the Oxford Term Loan. These expenses have been deferred, are included in other assets and are being expensed over the term of the Oxford Term Loan. No warrants were issued in connection with the Oxford Term Loan. The Company may prepay the full amount of the Oxford Term Loan, subject to prepayment premiums under certain circumstances. Oxford has the right to require the Company to prepay the full amount of the Oxford Term Loan if the Company prepays the full amount of the GECC Term Loan under certain circumstances.

The Oxford Term Loan is secured by certain laboratory and office equipment, furniture and fixtures acquired through September 30, 2010. In connection with the Oxford Term Loan, Oxford and GECC entered into a Lien Subordination Agreement, whereby GECC granted Oxford a first priority perfected security interest in the loan collateral. The Oxford Term Loan contains restrictive covenants, including the requirement for the Company to receive the prior written consent of Oxford to enter into acquisitions in which the Company incurs more than $2.0 million of related indebtedness, and customary default provisions that include material adverse events, as defined therein. The Company has determined that the risk of subjective acceleration under the material adverse events clause is remote and therefore has classified the outstanding principal in current and long-term liabilities based on the timing of scheduled principal payments.

Future minimum payments, excluding operating costs and taxes, under the Company's capital and non-cancellable operating leases and term loans are approximately as follows (in thousands):

	Operating leases	GECC Term Loan	Oxford Term Loan	Capital leases
Years ending December 31,				
2013	$ 2,162	$ 7,996	$ 813	$ 13
2014	2,160	4,863	271	1
2015	2,196	—	—	—
2016	1,965	—	—	—
Total minimum payments	$ 8,483	12,859	1,084	14
Less: amount representing interest		(1,459)	(96)	(0)
Present value of minimum payments		11,400	988	14
Less current portions of obligations		(7,200)	(724)	(13)
Long term obligation		$ 4,200	$ 264	$ 1

Rent expense under operating leases was approximately $2.2 million, $1.9 million and $2.0 million, for the years ended December 31, 2012, 2011 and 2010, respectively.

Guarantees

As permitted under Delaware law, the Company's Certificate of Incorporation and Bylaws provide that the Company will indemnify certain of its officers and directors for certain claims asserted against them in connection with their service as an officer or director. The maximum potential amount of future payments that the Company could be required to make under these indemnification provisions is

(10) Commitments and Contingencies (Continued)

unlimited. However, the Company has purchased a directors' and officers' liability insurance policy that reduces its monetary exposure and enables it to recover a portion of any future amounts paid. The Company believes the estimated fair value of these indemnification arrangements is minimal.

The Company customarily agrees in the ordinary course of its business to indemnification provisions in agreements with clinical trial investigators in its drug development programs, in sponsored research agreements with academic and not-for-profit institutions, in various comparable agreements involving parties performing services for the Company in the ordinary course of business, and in its real estate leases. The Company expects to agree to certain indemnification provisions in drug discovery and development collaboration agreements the Company may enter into. With respect to the Company's clinical trials and sponsored research agreements, these indemnification provisions typically apply to any claim asserted against the investigator or the investigator's institution relating to personal injury or property damage, violations of law or certain breaches of the Company's contractual obligations arising out of the research or clinical testing of the Company's compounds or drug candidates. With respect to lease agreements, the indemnification provisions typically apply to claims asserted against the landlord relating to personal injury or property damage caused by the Company, to violations of law by the Company or to certain breaches of the Company's contractual obligations. The indemnification provisions appearing in collaboration agreements are similar, but in addition provide some limited indemnification for the collaborator in the event of third-party claims alleging infringement of intellectual property rights. In each of the cases above, the term of these indemnification provisions generally survives the termination of the agreement, although the provision has the most relevance during the contract term and for a short period of time thereafter. The maximum potential amount of future payments that the Company could be required to make under these provisions is generally unlimited. The Company purchases insurance policies covering personal injury, property damage and general liability that reduce its exposure for indemnification and would enable it in many cases to recover a portion of any future amounts paid. The Company has never paid any material amounts to defend lawsuits or settle claims related to these indemnification provisions. Accordingly, the Company believes the estimated fair value of these indemnification arrangements is minimal.

(11) Related Party Transactions

The Company paid its scientific founder and a member of the board of directors consulting fees of $120,000 in each of the years ended in December 31, 2011 and 2010.

In April 2011, the Company sold an aggregate of 1,581,493 shares of common stock to certain of the Company's directors and entities affiliated with these directors at a purchase price of $4.89 per share in an issuer-directed registered direct offering (see Note 5).

In January 2012, the Company sold 1,136,363 shares of common stock to a director, who is its largest stockholder, at a purchase price of $4.40 per share in a public offering (see Note 5).

In July 2012, the Company entered into subscription agreements with certain directors, including its largest stockholder, pursuant to which the Company sold 3,976,702 shares of its common stock in a registered direct offering at a purchase price of $6.49 per share (see Note 5).

In November 2012, the Company purchased and retired 3,969 shares from an officer upon the vesting of restricted common stock in order to fund the related tax liability.

(11) Related Party Transactions (Continued)

In December 2012, the Company entered into common stock purchase agreements with certain directors, including its largest stockholder, pursuant to which the Company sold 2,649,535 shares of its common stock in a registered direct offering at a purchase price of $8.60 per share (see Note 5).

In January 2013, a director exercised an aggregate of 114,250 shares of common stock options that resulted in $1.0 million in proceeds to the Company.

(12) Retirement Plan

In 2003, the Company implemented a 401(k) retirement plan (the Synta 401(k) Plan) in which substantially all of its permanent employees are eligible to participate. Participants may contribute a percentage of their annual compensation to the plan, subject to statutory limitations. The Company may declare discretionary matching contributions to the Synta 401(k) Plan.

In April 2006, the Company began matching participants' contributions up to 50% of the first 6% of the employee's salary. The match is subject to a three-year equally graded vesting schedule and any forfeitures will be applied to reduce the Company's contributions. Company contributions for the years ended December 31, 2012, 2011 and 2010 were approximately$376,000, $372,000 and $429,000, respectively, subject to forfeitures.

(13) Quarterly Financial Data (unaudited)

The following tables present a summary of quarterly results of operations for 2012 and 2011:

	Three Months Ended			
	March 31, 2012	June 30, 2012	September 30, 2012	December 31, 2012
	(in thousands, except shares and per share data)			
Revenues:				
License and milestone revenue	$ —	$ —	$ —	$ —
Cost sharing reimbursements, net	—	—	—	—
Total collaboration revenues	—	—	—	—
Grant revenue	147	—	—	—
Total revenues	147	—	—	—
Operating expenses:				
Research and development	12,066	11,252	11,743	14,351
General and administrative	2,646	2,882	2,796	3,352
Total operating expenses	14,712	14,134	14,539	17,703
Loss from operations	(14,565)	(14,134)	(14,539)	(17,703)
Interest expense, net	(486)	(486)	(457)	(420)
Net loss	$ (15,051)	$ (14,620)	$ (14,996)	$ (18,123)
Basic and diluted net loss per common share	$ (0.27)	$ (0.25)	$ (0.25)	$ (0.29)
Basic and diluted weighted average number of common shares outstanding	56,366,992	57,650,412	60,661,720	62,914,546

(13) Quarterly Financial Data (unaudited) (Continued)

	Three Months Ended			
	March 31, 2011	June 30, 2011	September 30, 2011	December 31, 2011
	(in thousands, except shares and per share data)			
Revenues:				
License and milestone revenue	$ 1,143	$ 1,143	$ 1,143	$ 3,302
Cost sharing reimbursements, net	—	—	—	—
Total collaboration revenues	1,143	1,143	1,143	3,302
Grant revenue	—	211	521	121
Total revenues	1,143	1,354	1,664	3,423
Operating expenses:				
Research and development	9,436	10,417	10,751	10,859
General and administrative	2,673	2,946	3,131	2,803
Total operating expenses	12,109	13,363	13,882	13,662
Loss from operations	(10,966)	(12,009)	(12,218)	(10,239)
Interest expense, net	(435)	(493)	(516)	(504)
Net loss	$ (11,401)	$ (12,502)	$ (12,734)	$ (10,743)
Basic and diluted net loss per common share	$ (0.27)	$ (0.26)	$ (0.26)	$ (0.22)
Basic and diluted weighted average number of common shares outstanding	42,008,818	47,845,315	49,403,589	49,426,806

Exhibit 10.6.6

EXECUTION COPY

SIXTH AMENDMENT TO LOAN AND SECURITY AGREEMENT

THIS SIXTH AMENDMENT TO LOAN AND SECURITY AGREEMENT (this "**Amendment**") is dated as of December 6, 2012 and is effective as of the Amendment Effective Date (as defined in Section 5), by and among **SYNTA PHARMACEUTICALS CORP.**, a Delaware corporation ("**Borrower**"), **SYNTA SECURITIES CORP.**, a Massachusetts corporation ("**Guarantor**"; together with the Borrower, each a "**Loan Party**" and, collectively, the "**Loan Parties**"), **GENERAL ELECTRIC CAPITAL CORPORATION**, a Delaware corporation, acting in its capacity as agent ("**Agent**") for the lenders under the Loan Agreement (as defined below) (" **Lenders**"), and the Lenders.

W I T N E S S E T H:

WHEREAS, the Loan Parties, Lenders and Agent are parties to that certain Loan and Security Agreement, dated as of September 30, 2010 (as amended, restated, supplemented or otherwise modified from time to time, the " **Loan Agreement**"; capitalized terms used herein have the meanings given to them in the Loan Agreement except as otherwise expressly defined herein), pursuant to which Lenders have agreed to provide to Borrower certain loans and other extensions of credit in accordance with the terms and conditions thereof; and

WHEREAS, the Loan Parties have requested that Agent and Lenders amend certain provisions of the Loan Agreement, and Agent and Lenders are willing to grant such requests in accordance with, and subject to, the terms and conditions set forth herein.

NOW, THEREFORE, in consideration of the premises, the covenants and agreements contained herein, and other good and valuable consideration, the receipt and adequacy of which are hereby acknowledged, the Loan Parties, Lenders and Agent hereby agree as follows:

1. Acknowledgment of Obligations. Borrower hereby acknowledges, confirms and agrees that all Term Loans made prior to the date hereof, together with interest accrued and accruing thereon, and fees, costs, expenses and other charges owing by Borrower to Agent and Lenders under the Loan Agreement and the other Debt Documents, are unconditionally owing by Borrower to Agent and Lenders, without offset, defense or counterclaim of any kind, nature or description whatsoever except as may be limited by applicable bankruptcy, insolvency, reorganization, moratorium or other similar laws relating to or affecting creditor's rights generally.

2. Amendment to Loan Agreement. Subject to the terms and conditions of this Amendment, including, without limitation, the conditions precedent to effectiveness set forth in Section 5 below, Section 7.2(g) of the Loan Agreement is hereby amended by deleting such subsection in its entirety and substituting in lieu thereof the following:

> "(g) (i) Indebtedness owing by Borrower to Oxford Finance Corporation and any affiliates thereof that constitute an assignee or successor in interest to Oxford Finance Corporation (collectively, "Oxford") to finance existing equipment of the Borrower as of the Closing Date in an original principal amount not to exceed

$2,000,000; provided that the principal amount of such Indebtedness does not exceed the lower of the cost or fair market value of such equipment (the "Oxford Indebtedness") which Indebtedness is subject to that certain Lien Subordination Agreement, dated as of March 18, 2011 (the "Oxford Subordination Agreement") by and between Agent and Oxford in which Agent has subordinated its lien in such equipment to Oxford in accordance with the terms of the Oxford Subordination Agreement, and (ii) on and after December 6, 2012, additional Indebtedness owing by Borrower to Oxford to finance equipment purchases by the Borrower in an original principal amount not to exceed $600,000; provided, that, the principal amount of such Indebtedness does not exceed the lower of the cost or fair market value of such equipment (the "Additional Oxford Indebtedness"), which Additional Oxford Indebtedness is subject to the Oxford Subordination Agreement, as amended by that certain First Amendment to Lien Subordination Agreement by and between Agent and Oxford in which Agent has agreed to subordinate its lien in such equipment to Oxford in accordance with the terms of such Oxford Subordination Agreement, as so amended (which shall include Agent's discretion to review and approve in writing any supplements to Exhibit A of the Oxford Subordination Agreement in accordance therewith),"

3. No Other Consents or Amendments. Except for the amendment set forth and referred to in Sections 2 above, the Loan Agreement and the other Debt Documents shall remain unchanged and in full force and effect. Nothing in this Amendment is intended, or shall be construed, to constitute a novation or an accord and satisfaction of any of Borrower's or Guarantor's Obligations or to modify, affect or impair the perfection or continuity of Agent's security interests in, security titles to or other liens, for the benefit of itself and the Lenders, on any Collateral for the Obligations.

4. Representations and Warranties. To induce Agent and Lenders to enter into this Amendment, each Loan Party does hereby warrant, represent and covenant to Agent and Lenders that after giving effect to this Amendment (a) each representation or warranty of the Loan Parties set forth in the Loan Agreement is hereby restated and reaffirmed as true and correct in all material respects (without duplication of any materiality qualifier contained therein) on and as of the date hereof as if such representation or warranty were made on and as of the date hereof (except to the extent that any such representation or warranty expressly relates to a prior specific date or period), (b) no Default or Event of Default has occurred and is continuing as of the date hereof and (c) each Loan Party has the power and is duly authorized to enter into, deliver and perform this Amendment and this Amendment is the legal, valid and binding obligation of each Loan Party enforceable against each Loan Party in accordance with its terms.

5. Conditions Precedent to Effectiveness of this Amendment. This Amendment shall become effective as of the date hereof (the "**Amendment Effective Date**") upon satisfaction of the following conditions:

(a) Agent shall notify Borrower in writing that Agent has received one or more counterparts of this Amendment duly executed and delivered by the Loan Parties, Agent and Lenders, in form and substance satisfactory to Agent and Lenders;

(b) Both before and after giving effect to this Amendment, no Default or Event of Default shall have occurred and be continuing; and

(c) Agent shall have received all other documents and instruments as Agent or any Lender may reasonably deem necessary or appropriate to effectuate the intent or purpose of this Amendment.

6. Release.

(a) In consideration of the agreements of Agent and Lenders contained herein and for other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, each Loan Party, on behalf of itself and its successors, assigns, and other legal representatives, hereby absolutely, unconditionally and irrevocably releases, remises and forever discharges Agent and each Lender and their respective successors and assigns, and their respective present and former shareholders, affiliates, subsidiaries, divisions, predecessors, directors, officers, attorneys, employees, agents and other representatives (Agent, Lenders and all such other persons being hereinafter referred to collectively, as the " **Releasees**" and individually, as a "**Releasee**"), of and from all demands, actions, causes of action, suits, covenants, contracts, controversies, agreements, promises, sums of money, accounts, bills, reckonings, damages and any and all other claims, counterclaims, defenses, rights of set-off, demands and liabilities whatsoever (individually, a " **Claim**" and collectively, "**Claims**") of every name and nature, known or unknown, suspected or unsuspected, both at law and in equity, which any Loan Party or any of its respective successors, assigns, or other legal representatives may now or hereafter own, hold, have or claim to have against the Releasees or any of them for, upon, or by reason of any circumstance, action, cause or thing whatsoever which arises at any time on or prior to the Amendment Effective Date, including, without limitation, for or on account of, or in relation to, or in any way in connection with the Loan Agreement or any of the other Debt Documents or transactions thereunder or related thereto.

(b) Each Loan Party understands, acknowledges and agrees that its release set forth above may be pleaded as a full and complete defense and may be used as a basis for an injunction against any action, suit or other proceeding which may be instituted, prosecuted or attempted in breach of the provisions of such release.

(c) Each Loan Party agrees that no fact, event, circumstance, evidence or transaction which could now be asserted or which may hereafter be discovered shall affect in any manner the final, absolute and unconditional nature of the release set forth above.

7. Covenant Not To Sue. Each Loan Party, on behalf of itself and its respective successors, assigns, and other legal representatives, hereby absolutely, unconditionally and irrevocably, covenants and agrees with and in favor of each Releasee that it will not sue (at law, in equity, in any regulatory proceeding or otherwise) any Releasee on the basis of any Claim

released, remised and discharged by the Loan Parties pursuant to Section 6 above. If any Loan Party or any of its respective successors, assigns or other legal representatives violates the foregoing covenant, each Loan Party, for itself and its successors, assigns and legal representatives, jointly and severally agrees to pay, in addition to such other damages as any Releasee may sustain as a result of such violation, all attorneys' fees and costs incurred by any Releasee as a result of such violation.

8. Advice of Counsel. Each of the parties represents to each other party hereto that it has discussed this Amendment with its counsel.

9. Severability of Provisions. In case any provision of or obligation under this Amendment shall be invalid, illegal or unenforceable in any applicable jurisdiction, the validity, legality and enforceability of the remaining provisions or obligations, or of such provision or obligation in any other jurisdiction, shall not in any way be affected or impaired thereby.

10. Counterparts. This Amendment may be executed in multiple counterparts, each of which shall be deemed to be an original and all of which when taken together shall constitute one and the same instrument.

11. GOVERNING LAW. THIS AMENDMENT SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH, THE INTERNAL LAWS OF THE STATE OF NEW YORK APPLICABLE TO CONTRACTS MADE AND PERFORMED IN SUCH STATE WITHOUT REGARD TO THE PRINCIPLES THEREOF REGARDING CONFLICTS OF LAWS.

12. Entire Agreement. The Loan Agreement as and when amended through this Amendment embodies the entire agreement between the parties hereto relating to the subject matter thereof and supersedes all prior agreements, representations and understandings, if any, relating to the subject matter thereof.

13. No Strict Construction, Etc. The parties hereto have participated jointly in the negotiation and drafting of this Amendment. In the event an ambiguity or question of intent or interpretation arises, this Amendment shall be construed as if drafted jointly by the parties hereto and no presumption or burden of proof shall arise favoring or disfavoring any party by virtue of the authorship of any provisions of this Amendment. Time is of the essence for this Amendment.

14. Costs and Expenses. Loan Parties absolutely and unconditionally agree, jointly and severally, to pay or reimburse upon demand for all reasonable fees, costs and expenses incurred by Agent and the Lenders that are Lenders on the Closing Date in connection with the preparation, negotiation, execution and delivery of this Amendment and any other Debt Documents or other agreements prepared, negotiated, executed or delivered in connection with this Amendment or transactions contemplated hereby.

[Signature Pages Follow]

IN WITNESS WHEREOF, the parties hereto have caused this Sixth Amendment to Loan and Security Agreement to be duly executed and delivered as of the day and year specified at the beginning hereof.

BORROWER:

SYNTA PHARMACEUTICALS CORP.

By: /s/ Keith Ehrlich
Name: Keith Ehrlich
Title: CFO

GUARANTOR:

SYNTA SECURITIES CORP.

By: /s/ Keith Ehrlich
Name: Keith Ehrlich
Title: Director

AGENT AND LENDER:

GENERAL ELECTRIC CAPITAL CORPORATION

By: /s/ Alan M. Silbert
Name: Alan M. Silbert
Title: Its Duly Authorized Signatory

LENDER:

MIDCAP FUNDING III, LLC

By: /s/ Luis Viera
Name: Luis Viera
Title: Managing Director

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement (Form S-3 No. 333-176022) of Synta Pharmaceuticals Corp., the Registration Statement (Form S-8 No. 333-141903) pertaining to the 2001 Stock Plan, the 2006 Stock Plan and the Non-qualified Stock Option Agreement dated May 27, 2004, the Registration Statement (Form S-8 No. 333-152824) pertaining to the Amended and Restated 2006 Stock Plan, and the Registration Statement (Form S-8 No. 333-173862) pertaining to the Amended and Restated 2006 Stock Plan of Synta Pharmaceuticals Corp., and the Registration Statement (Form S-8 No. 333-181117) pertaining to the Amended and Restated 2006 Stock Plan of Synta Pharmaceuticals Corp., of our reports dated March 14, 2013, with respect to the consolidated financial statements of Synta Pharmaceuticals Corp. and the effectiveness of internal control over financial reporting of Synta Pharmaceuticals Corp. included in this Annual Report (Form 10-K) for the year ended December 31, 2012.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 14, 2013

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Exhibit 31.1

CERTIFICATIONS UNDER SECTION 302

I, Safi R. Bahcall, Ph.D., certify that:

1. I have reviewed this Annual Report on Form 10-K of Synta Pharmaceuticals Corp.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 14, 2013

/s/ SAFI R. BAHCALL

Safi R. Bahcall, Ph.D.
President and Chief Executive Officer
(principal executive officer)

QuickLinks

QuickLinks -- Click here to rapidly navigate through this document

Exhibit 31.2

CERTIFICATIONS UNDER SECTION 302

I, Keith S. Ehrlich, certify that:

1. I have reviewed this Annual Report on Form 10-K of Synta Pharmaceuticals Corp.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Dated: March 14, 2013

/s/ KEITH S. EHRLICH

Keith S. Ehrlich, C.P.A.
Vice President, Finance and Administration,
Chief Financial Officer
(principal accounting and financial officer)

QuickLinks

Exhibit 32.1

CERTIFICATIONS UNDER SECTION 906

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), each of the undersigned officers of Synta Pharmaceuticals Corp., a Delaware corporation (the "Company"), does hereby certify, to such officer's knowledge, that:

The Annual Report on Form 10-K for the year ended December 31, 2012 (the "Form 10-K") of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: March 14, 2013

/s/ SAFI R. BAHCALL

Safi R. Bahcall, Ph.D.
President and Chief Executive Officer
(principal executive officer)

Dated: March 14, 2013

/s/ KEITH S. EHRLICH

Keith S. Ehrlich, C.P.A.
Vice President, Finance and Administration,
Chief Financial Officer
(principal accounting and financial officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

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