



	LEAD OPT	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
ONCOLOGY					
Ganetespib Hsp90 Inhibitor					
Non-Small Cell Lung Cancer Ph 2b/3					
Non-Small Cell Lung Cancer					
Gastrointestinal Stromal Tumors					
Colorectal Cancer		-			
Gastric Cancer		-			
Small Cell Lung Cancer		 	-		
Ocular Melanoma					
Hematologic Malignancies		1			
Pancreatic Cancer			-		
Prostate Cancer					
Breast Cancer					
Hepatocellular Cancer (Phase 1/2)					
Docetaxel Combination in Solid Tumors					
Solid/Hematologic (3 trials)					
Elesciomol Mitochondria Metabolism In	hibitor				
Non-Small Cell Lung Cancer			fe in Si tablen in Sinta and Sinta and		
Ovarian Cancer					
Acute Myeloid Leukemia		1			
STA-9584 Vascular Disrupting Agent					
INFLAMMATION					
CRACM Ion Channel Inhibitor					
IL-12/23 Inhibitors					

#### TO OUR SHAREHOLDERS



In 2010 we established an exciting platform for delivering on our long-term mission to extend and enhance the lives of patients: two advanced-stage drug candidates with strong clinical data, first-in-class or best-in-class mechanisms, in over 15 trials including lung, colon, prostate, breast, ovarian, and gastric cancer.

#### Ganetespib: Best-In-Class Hsp90 Inhibitor

Ganetespib, our Hsp90 inhibitor, emerged as a potentially best-inclass compound, with exciting clinical results and broad support among key opinion leaders, reflected in our large and growing number of investigator-sponsored or foundation-sponsored trials.

Hsp90 is a pathway that large and small companies have attempted to target before, given the strong scientific rationale and the encouraging preclinical and clinical data from first-generation compounds. First-generation compounds, however, suffered from liver toxicity issues and weak potency. To succeed, a next-generation compound has to achieve three goals: improved potency, improved safety, and demonstration of clear single-agent clinical activity. Because the opportunity is tremendous — broad, multi-tumor application and the potential to form a cornerstone of combination therapy, given the known ability of Hsp90 inhibition to suppress mechanisms of resistance to other therapies — a number of companies, including Synta, began research in this area several years ago.

This past year we showed that ganetespib is the first compound to achieve the three goals. Compounds in development by other pharmaceutical companies showed high eye toxicities, whereas ganetespib showed a favorable safety profile and demonstrated clear clinical activity. With over 350 patients treated and eleven ongoing Phase 2 trials the data are clear: ganetespib has the potential to be the first Hsp90 inhibitor to market.

This is an exciting achievement for the field and for patients – and a tremendous opportunity for Synta. We intend to move quickly and strategically to maintain and extend our advantages in this area. We recently announced a Phase 2b/3 trial in lung cancer, which we expect to initiate in Q2 2011, and you can expect more announcements over the course of this year related to our plans in other cancers and for establishing ganetespib as a foundation of combination therapy – as an enhancer of chemotherapy, of certain targeted agents, and of radiotherapy.

#### **Elesclomol: Targeting Energy Production in Cancer Cells**

Elesclomol is our first-in-class mitochondria metabolism inhibitor. This compound acts in an entirely different manner than nearly all standard anti-cancer treatments: it is neither a chemotherapy, which disrupts cell division, nor is it an agent that targets growth factors or cell signaling factors. Elesclomol targets the power plants of cancer cells – the mitochondria. In 2010, our scientists made an important discovery: a way to identify in advance those patients who are most likely to benefit from eleslcomol. The level of a certain enzyme, related to mitochondrial energy production, correlates with activity of elesclomol in the lab. In three randomized trials, involving over 800 patients, elesclomol showed the same pattern – activity in patients with this "biomarker"; absence of any benefit in patients without the biomarker. All of our ongoing and planned trials with eleslcomol incorporate use of this marker.

We and our collaborators are excited to pioneer an entirely new approach to treating cancer, with an equally novel way to identify those patients most likely to benefit. You can expect to hear much more about both the novel science, and new clinical trials for this program, over the coming year.

#### The Path Forward

I would like to close with one of a now increasing number of stories we hear from our clinical trials. A 67-year old man with advancedstage lung cancer had been in pain a long time and had been through four widely used therapies for this disease – carboplatin, Taxol, Avastin, Sutent – with no improvement. The patient enrolled in our Phase 2 lung cancer trial in the fall of 2010. Two weeks after administering the first dose of ganetespib, the physician reported to us that the patient's wife called his office. Her message: "Thank you for giving me my husband back." He was out of pain for the first time. His first scan soon after showed 35% tumor shrinkage – an objective response.

At Synta, stories like the one above inspire all of us, every day – and we work hard to realize the potential of our promising therapies to benefit patients.

I expect the coming year to be transformational, as we begin pivotal trials, receive and report on results from ongoing programs, and potentially enter into one or more partnerships for our drug candidates.

We are grateful for your continued interest in and support of Synta, and its mission of enhancing the lives of patients with severe medical conditions.

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



**Ganetespib** (formerly STA-9090) is a potent, synthetic, small-molecule inhibitor of heat shock protein 90 (Hsp90). Hsp90 is a molecular chaperone required for the proper folding and activation of many cancer-promoting proteins, and is recognized as a key facilitator of cancer cell growth and survival. In preclinical experiments, ganetespib has shown activity in multiple tumor models both as a single agent and in combination with certain widely used anti-cancer agents including chemotherapy, radiotherapy, targeted agents and hormone therapy. Ganetespib is currently being evaluated in a broad range of cancer clinical trials. In these trials, ganetespib has demonstrated clinical activity in heavily pretreated patients and has been well tolerated to date with no evidence of severe liver or common ocular toxicities seen with other Hsp90 inhibitors. The most common adverse event seen to date has been diarrhea, which has been manageable with standard supportive care. A Phase 2b/3 twain non-small cell lung cancer is expected to initiate in Q2, 2011 with additional trials expected to start in the second half of the year.



PHASE 2b/3 TRIAL: Ganetespib in Non-Small Cell Lung Cancer (NSCLC)

» Synta Pharmaceuticals

PHASE 2 TRIAL: Ganetespib in Non-Small Cell Lung Cancer (NSCLC) » Synta Pharmaceuticals

PHASE 2 TRIAL: Ganetespib in Gastrointestinal Stromal Tumors (GIST)

» Synta Pharmaceuticals

## PHASE 2 TRIAL: Ganetespib in Colorectal Cancer

» Memorial Sloan-Kettering Cancer Center

# PHASE 2 TRIAL: Ganetespib in **Gastric Cancer**

- » Massachusetts General Hospital
- » Dana-Farber Cancer Institute
- » Beth Israel Deaconess Medical Center

# PHASE 2 TRIAL: Ganetespib in Small Cell Lung Cancer

- » Massachusetts General Hospital
- » Beth Israel Deaconess Medical Center

# PHASE 2 TRIAL: Ganetespib in Ocular Melanoma

- » Beth Israel Deaconess Medical Center
- » Massachusetts General Hospital
- » Brigham and Women's Hospital

# PHASE 2 TRIAL: Ganetespib in **Pancreatic Cancer**

- » Vanderbilt-Ingram Cancer Center
- » National Cancer Institute (NCI)

# PHASE 2 TRIAL: Ganetespib in **Prostate Cancer**

- » Barbara Ann Karmanos Cancer Institute
- » National Cancer Institute (NCI)



# PHASE 2 TRIAL: Ganetespib in Breast Cancer » Memorial Sloan-Kettering Cancer Center

# PHASE 1/2 TRIAL: Ganetespib in Acute Myeloid Leukemia (AML)

» Synta Pharmaceuticals

# PHASE 1 TRIAL: Ganetespib in Combination with Docetaxel in

#### Solid Tumors

» Synta Pharmaceuticals

# Phase 1 Trial: Ganetespib in Hepatocellular Cancer

» Massachusetts General Hospital

- » Dana Farber/Partners Cancer Care
- » Beth Israel Deaconess Medical Center

Elesciomol is a first-in-class, investigational drug candidate that triggers programmed cell death (apoptosis) in cancer cells through a novel mechanism: disrupting mitochondrial energy metabolism. Because elesclomol targets active mitochondrial metabolism, anti-cancer activity is seen only in the normoxic - normal oxygen metabolic state; not in the hypoxic - insufficient oxygen - metabolic state. In three randomized clinical trials elesclomol has shown clinical activity in patients whose cancers show a signature characteristic ("biomarker") of the normoxic metabolic state. Clinical trials in leukemia and ovarian cancer are ongoing; a trial in lung cancer is expected to initiate later this year. Elesclomol represents an entirely novel way to treat cancer, with an innovative approach to identifying only those patients likely to benefit from treatment.

# PHASE 1 TRIAL: Elesclomol in Acute Myeloid Leukemia (AML)

- » Memorial Sloan Kettering Cancer Center
- » Princess Margaret Hospital (Toronto, Canada)

PHASE 2 TRIAL: Elesclomol in Combination with Paclitaxel in

# **Ovarian Cancer**

- » Gynecologic Oncology Group
- » National Cancer Institute (NCI)

PHASE 2 TRIAL: Elesclomol in Combination with Paclitaxel in

Non-Small Cell Lung Cancer (NSCLC)

» Synta Pharmaceuticals

#### SENIOR MANAGEMENT

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

Keizo Koya, Ph.D. Senior Vice President, Pharmaceutical Development

Amar Singh Senior Vice President, Chief Business Officer

Vojo Vukovic, M.D., Ph.D. Senior Vice President, Chief Medical Officer

Suresh Babu, Ph.D. Vice President, Drug Product Development

Keith Ehrlich, C.P.A. Vice President, Finance and Administration Chief Financial Officer

Iman El-Hariry, M.D., Ph.D. Vice President, Clinical Research

**Rob Kloppenburg** Vice President, Investor Relations and Corporate Communications

Arthur McMahon Vice President, Human Resources

Wendy Rieder, Esq. Vice President, Intellectual Property and Legal Affairs General Counsel

Andrew Sonderfan, Ph.D., DABT Vice President, Drug Disposition and Preclinical Safety

#### BOARD OF DIRECTORS

Keith Gollust (Chairman) President, Gollust Management

Safi Bahcall, Ph.D. Synta Pharmaceuticals Corp.

Lan Bo Chen, Ph.D. Harvard University and Dana-Farber Cancer Institute (Emeritus)

Bruce Kovner Chairman, Caxton Corp.

**Donald Kufe, M.D.** Dana-Farber Cancer Center

William Reardon, C.P.A. PricewaterhouseCoopers (ret)

**Robert Wilson** Vice Chairman, Board of Directors Johnson & Johnson (ret)

#### TRANSFER AGENT

Computershare P.O. Box 43023 Providence, RI 02904 Phone: 800-662-7232 The Transfer Agent is responsible for handling shareholder questions regarding lost certificates, address changes and changes of ownership or name in which shares are held.

#### INDEPENDENT ACCOUNTANTS

Ernst & Young LLP 200 Clarendon Street Boston, MA 02116

#### CORPORATE COUNSEL

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. One Financial Center Boston, MA 02111 Phone: 617-542-6000 Fax: 617-542-2241

MARKET FOR SYNTA PHARMACEUTICALS CORP. COMMON STOCK

Nasdaq Global Market: SNTA

#### INVESTOR INFORMATION

Copies of our annual reports on Form 10-K, proxy statements, quarterly reports on Form 10-Q, and current reports on Form 8-K are available to stockholders upon request without charge. Please visit our website at **www.syntapharma.com** or send requests to:

#### **Investor Relations**

Synta Pharmaceuticals Corp. 45 Hartwell Avenue Lexington, MA 02421 Phone: 781-541-7125 Fax: 781-274-1270 E-mail: ir@syntapharma.com

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## Investors

For access to Synta Pharmaceuticals Annual Meeting materials using your smart phone, scan this quick response (QR) code. Here you can view the 2010 Form 10-K and Notice of 2011 Annual Meeting and Proxy Statement.

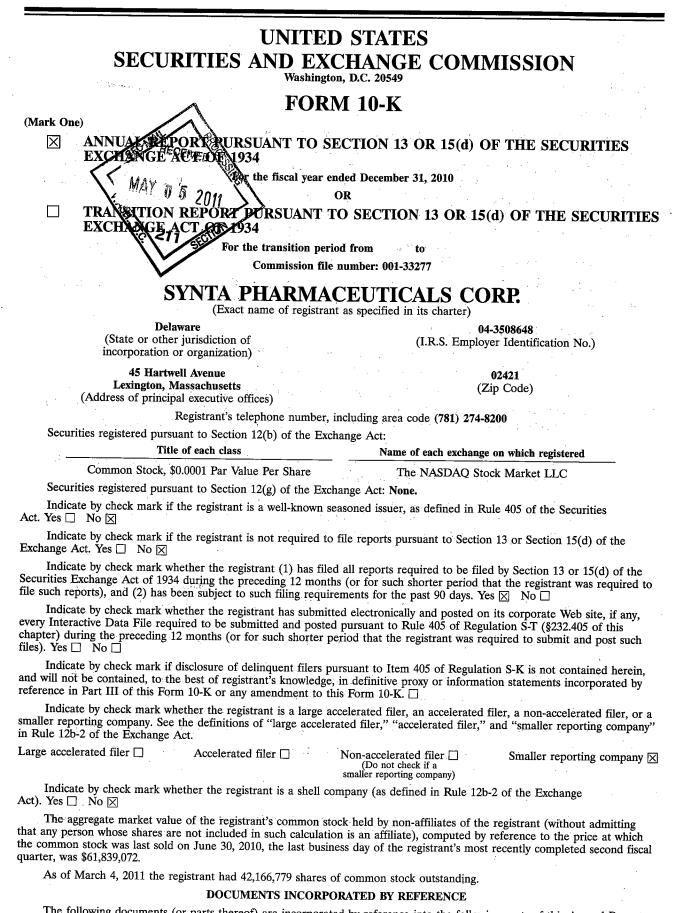


#### SAFE HARBOR STATEMENT

This annual report contains forward-looking statements about Synta Pharmaceuticals Corp. Such forward-looking statements can be identified by the use of forward-looking terminology such as "will", "would", "should", "expects", "anticipates", "intends", "plans", "believes", "may", "estimates", "predicts", "projects", or similar expressions intended to identify forward-looking statements. Such statements, including statements relating to the timing and progress of our clinical and preclinical programs, and our strategic plans, reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such forward-looking statements, including those described in the "Risk Factors" section of our Form 10-K for the year ended December 31, 2010 as filed with the Securities and Exchange Commission. Synta undertakes no obligation to publicly update forward-looking statements, whether because of new information, future events or otherwise, except as required by law.



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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 2011 Annual Meeting of Stockholders to be held on May 26, 2011.

#### 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. Each of our drug candidates was discovered and developed internally using our proprietary, unique chemical compound library and integrated discovery engine. We have granted Hoffman-La Roche, or Roche, an exclusive license to develop and commercialize certain compounds from our calcium release activated calcium modulator, or CRACM, program resulting from our research partnership with them. We retain full ownership of all of our other drug candidates.

In 2010, we made significant progress in advancing our drug candidates and achieved a number of other important milestones in our other programs, including:

#### Ganetespib (formerly STA-9090)

- Initiated multiple new Phase 2 trials at leading academic centers and achieved a cumulative total enrollment of over 350 patients across all of our trials.
- Demonstrated that ganetespib as a single agent can induce durable tumor responses and sustained tumor shrinkage in heavily pre-treated patients with advanced lung cancer, breast cancer, gastric cancer, colorectal cancer, renal cancer, melanoma and Gleevec-resistant gastrointestinal stromal tumors, or GIST.
- Showed a favorable safety profile with no evidence of the serious liver and common ocular toxicities seen with other Hsp90 inhibitors.
- Developed plans for a multi-national, randomized, registration-enabling Phase 2b/3 clinical trial of ganetespib in combination with docetaxel in non-small cell lung cancer, or NSCLC, to begin in the second quarter of 2011.

#### Elesclomol

- Initiated a clinical trial of elesclomol in combination with paclitaxel in advanced ovarian cancer, being conducted by the Gynecological Oncology Group and supported by the National Cancer Institute.
- Initiated a single agent, dose optimization clinical trial of elesclomol in acute myeloid leukemia, or AML.
- Established strong scientific and clinical evidence that lactate dehydrogenase, or LDH, is a predictive biomarker for clinical activity of elesclomol, i.e., that level of LDH can serve to identify those patients most likely to derive benefit from treatment with elesclomol. Incorporated use of this biomarker into all ongoing and planned trials for elesclomol.
- Developed plans for a multi-national randomized clinical trial in NSCLC to start in the second quarter of 2011.

#### Other

• Completed the research term of our collaboration with Roche, exclusively licensing several CRACM inhibitor compounds to Roche for further preclinical and clinical development.

- Received a funding commitment from the Multiple Myeloma Research Foundation, or MMRF, of up to \$1 million to support a clinical trial of ganetespib in combination with bortezomib (Velcade) in multiple myeloma.
- Received four awards totaling approximately \$1 million under the US Internal Revenue Service Qualifying Therapeutic Discovery Project program.
- Received a \$1 million funding recommendation from the Department of Defense, or DoD, to advance studies of our vascular disrupting agent, or VDA, STA-9584 against advanced prostate cancer.

We believe that our competitive advantages include:

- the broad clinical and commercial potential of our drug candidates;
- the strength of our intellectual property portfolio, consisting of over 700 issued and pending patents;
- our proprietary chemical compound library and the strength of our drug discovery platform, with which we have generated all of our drug candidates;
- our ability to integrate discovery, translational, and clinical research to optimize our scientific and clinical choices and further strengthen our intellectual property position;
- our operational experience in effectively managing large-scale global clinical programs;
- the full ownership of our programs, which creates strategic flexibility in partnership discussions that can be used to enhance the value we may ultimately capture from our drug candidates;
- our strong network of relationships with leading investigators and institutions, which facilitates our ability to conduct clinical trials efficiently; and
- the skills, talent, and level of industry experience of our employees.

We believe that these competitive advantages provide us with multiple, sustainable growth opportunities.

#### **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:

- 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;
- 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; and

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

## **Our Drug Candidate Pipeline**

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

	Product Candidate	Disease	Stage	Development State
ncology	Ganetespib Hsp90 inhibitor			, , , , , , , , , , , , , , , , , , ,
	(Company-Sponsored Phase 2, Phase 3 Trials)	Non-small cell lung cancer	Phase 2b/3	Expect to initiate i Q2 2011
. t. t		Non-small cell lung cancer	Phase 2	Ongoing
		Gastrointestinal stromal tumors	Phase 2	Ongoing
s stations.	en de la companya de La companya de la comp	Hematologic cancers (once per week administration)	Phase 1/2	Ongoing
·	(Investigator-Sponsored Phase 2 Trials)	Colorectal cancer	Phase 2	Ongoing
		Gastric cancer	Phase 2	Ongoing
		Small cell lung cancer	Phase 2	Ongoing
		Ocular melanoma	Phase 2	Ongoing
<b>`</b>		Pancreatic cancer	Phase 2	Ongoing
		Prostate cancer	Phase 2	Ongoing
		Breast cancer	Phase 2	Ongoing
		Hepatocellular (liver) cancer	Phase 1/2	Ongoing
	(Phase 1 trials)	Solid tumors in combination with docetaxel	Phase 1	Ongoing
		Hematologic cancers (twice per week administration)	Phase 1	Ongoing
		Solid tumors (once per week administration)	Phase 1	Ongoing
		Solid tumors (twice per week administration)	Phase 1	Ongoing
a An an an an an	Additional Hsp90 inhibitors	Cancer	Preclinical development	Ongoing
_	Elesclomol Mitochondria-targeting agent	Non-small cell lung cancer	Phase 2b	Expect to initiat Q2 2011
		Ovarian cancer	Phase 2	Ongoing
	$(g_{1},\ldots,g_{n})^{T} \in \{0,\ldots,M^{T}\}$	Acute myeloid leukemia	Phase 1	Ongoing
	STA-9584 Vascular disrupting agent	Prostate cancer	Preclinical development	Ongoing
nflammatory Diseases	CRACM channel inhibitors	Autoimmune diseases Respiratory conditions Transplant	Preclinical development	
	IL-12/23 inhibitors	Autoimmune diseases	Lead optimization	Ongoing
· · · ·			1. J. C	

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We have granted Roche an exclusive license to develop and commercialize certain compounds from our CRACM program resulting from our research partnership with them, which ended in December 2010. We retain full ownership of all of our other 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 full 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 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, for example tyrosine kinases, that drive the growth, proliferation, and survival of many different types of cancer. Ganetespib is structurally unrelated to the ansamycin family of first-generation Hsp90 inhibitors (such as 17-AAG and IPI-504) and has shown superior activity to these agents in preclinical studies. Ganetespib is currently being evaluated in eleven Phase 2 clinical trials, with several additional trials expected to initiate in 2011, both as a single agent, or monotherapy, and in combination with other therapies. We expect to initiate a randomized, Phase 2b/3 NSCLC clinical trial in combination with docetaxel, which is designed to be registration-enabling, in the second quarter of 2011.
- *Elesclomol, mitochondria-targeting agent.* Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death, or apoptosis, in cancer cells by disrupting cancer cell mitochondrial metabolism. Results from three randomized clinical trials and subsequent research have established that patient baseline serum level of LDH is an important predictor of elesclomol treatment outcome. Elesclomol is currently in a clinical trial in ovarian cancer in combination with paclitaxel and a clinical trial in AML as a single agent. We expect to begin one or more new trials with elesclomol in 2011, including a randomized Phase 2b clinical trial in NSCLC.
- STA-9584, vascular disrupting agent. STA-9584, our novel, injectable, small molecule compound that appears to disrupt the blood vessels that supply tumors with oxygen and essential nutrients, is in preclinical development. The DoD has recommended a \$1 million grant to advance the investigation of STA-9584 against advanced prostate cancer. We expect to begin studies supported by this grant in the first half of 2011.

#### **Oncology Background**

Cancers are diseases characterized by abnormal and uncontrolled cell growth and division, typically leading to tumor formation. As a tumor grows, it can directly disrupt organ function at its site of origin. In addition, cancer cells can also spread to other organs, such as the brain, bones and liver, by a process called metastasis. 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 1.5 million people in the United States were diagnosed with cancer in 2009, and approximately 562,000 people will die from the disease.

According to a 2009 IMS health report, oncology products are the largest therapeutic class of pharmaceuticals in the world with global sales of \$52.4 billion in 2009.

#### Ganetespib (Hsp90 Inhibitor)

Ganetespib is a potent, synthetic inhibitor of Hsp90. Many of the known oncogenic proteins that play major roles in pathogenesis of solid tumor and hematologic malignancies are client proteins of Hsp90. By inhibiting Hsp90, ganetespib causes the degradation of these client proteins and the subsequent death of cancer cells dependent on these proteins. Ganetespib has shown potent anticancer activity in a broad range of solid and hematologic cancers both *in vitro* and *in vivo*, including cancers resistant to targeted agents and chemotherapies.

In clinical trials to date, ganetespib has shown encouraging evidence of clinical activity, including prolonged tumor shrinkage in patients who have progressed after, or failed to respond to, treatment with commonly-used drugs for these tumors. Currently, over 350 patients have been treated with ganetespib across all trials. Ganetespib has been well tolerated to date, with no evidence of the serious liver or common ocular toxicities seen with other Hsp90 inhibitors. The most common adverse event seen with ganetespib is diarrhea, which has been manageable and reversible with standard supportive care.

# Ganetespib's Mechanism of Action

Ganetespib potently inhibits Hsp90, a chaperone protein required for the proper folding and activation of other cellular proteins, particularly kinases. Many of these "client proteins" of Hsp90—such as AKT, BCR-ABL, BRAF, KIT, MET, EGFR, FLT3, HER2, PDGFRA, VEGFR—have been shown to be critical to cancer cell growth, proliferation, and survival and are the targets of clinically validated and approved cancer drugs, such as Gleevec, Avastin, Herceptin, Sutent, Nexavar, Tarceva, and Erbitux. In preclinical studies, inhibiting Hsp90 causes the degradation of multiple client proteins and leads to cancer cell death.

#### Ganetespib Preclinical Results

Experiments conducted by us and by our collaborators at the Dana-Farber Cancer Institute, Brigham and Women's Hospital in Boston, University of Massachusetts Medical School in Worcester, The Ohio State University, University of Texas Health Center at San Antonio, and others have shown that ganetespib:

- potently inhibits many critical oncogenic proteins including HIF1alpha, KIT, MET, HER2, EGFR, AKT, CDK4, BCR-ABL, BRAF, RAF1, and WT1;
- is active against a broad range of *in vivo* models of cancer including breast, colon, gastric, lung, GIST, melanoma, osteosarcoma, prostate, AML, chronic myeloid leukemia, Burkitt's lymphoma, diffuse large B-cell lymphoma, and multiple myeloma;
- is active in models that are non-responsive or resistant to first-generation Hsp90 inhibitors, such as 17-AAG;

- persists selectively in tumors, with a tumor half-life up to 20 times longer in duration than the half-life in plasma or normal tissues such as lung or liver;
- demonstrates complementary anti-cancer activity, or synergy, with several widely-used anti-cancer therapies including Taxol, Tarceva, and Avastin;
- has activity in models of cancer that have become resistant to approved tyrosine kinase inhibitors such as Gleevec, Sutent, Tarceva, and Sprycel—including the BCR-ABL T315I mutation in leukemia; the EGFR T790M mutation in lung cancer; and the KIT V654A or D820A mutations in GIST; and
- in prodrug form, generated pronounced single-agent tumor responses in a canine clinical trial, including over 80% tumor shrinkage in dogs with certain rapidly progressing cancers.

#### Ganetespib Clinical Trials

#### Phase 1 Clinical Trials

We initiated a series of Phase 1, open-label trials in patients with solid-tumor and hematologic cancers to identify the maximum tolerated dose, or MTD, of ganetespib based on once-weekly and twice-weekly intravenous dosing schedules. Preliminary results were presented at the meeting of the American Society of Clinical Oncology, or ASCO, 2010 for the solid-tumor trials and at the meeting of the American Society of Hematology, or ASH, 2010 for the hematologic cancer trials.

We observed encouraging signs of clinical activity in these trials including durable tumor shrinkage or confirmed Response Evaluation Criteria in Solid Tumors, or RECIST, responses in patients with lung cancer, renal cancer, Gleevec-resistant GIST, melanoma, triple-negative breast cancer and colorectal cancer. These patients had progressed on, or failed to respond to, numerous prior therapies, including chemotherapies such as carboplatin and paclitaxel, and targeted agents such as Avastin, Sutent, Gleevec and Tarceva. Certain patients have remained on treatment with ganetespib for over one year.

A maximum tolerated dose of  $216 \text{ mg/m}^2$  was established in the solid tumor Phase 1 study with once-weekly dosing schedule and  $200 \text{ mg/m}^2$  was chosen as the recommended Phase 2 dose. The most commonly reported adverse event across these trials was diarrhea, which was manageable and reversible. There was no evidence of the serious liver or common ocular toxicities seen with other Hsp90 inhibitors.

#### Phase 2 Clinical Trials

In December 2009, we initiated a Phase 2 trial for ganetespib, administered as monotherapy in patients with advanced NSCLC who have progressed on, or failed to respond to, prior treatments. In September 2010, we announced the expansion of this trial from up to 69 patients to up to 146 patients. We decided to expand the trial based on encouraging activity observed in the first stage of the two stage clinical trial in patients having tumors with a specific genetic profile, namely the EGFR and KRAS wild type mutational status. In addition, a new patient cohort was created to allow certain patients from the trial who had received treatment with ganetespib and were showing a mixed response—for example, shrinkage of certain tumor lesions, but growth of other tumor lesions—to continue treatment with ganetespib while adding treatment with docetaxel to the regimen.

In February 2011, we presented preliminary results from patients with EGFR and KRAS wild type tumors. Of 33 evaluable patients, 22 showed target lesion stabilization (growth <20% at 8 weeks); 10 showed target lesion tumor shrinkage; and three showed confirmed partial responses per RECIST criteria (target lesion shrinkage >30%). The observed tumor responses were durable, with the three patients all continuing to receive treatment, two having been on treatment for six months and one for fourteen months. We believe that these results demonstrate that ganetespib is clinically active, as a single agent, in patients with advanced relapsed or refractory NSCLC.

A favorable safety profile was also observed in this patient population. The highest incidence of treatment-related grade 3 or 4 adverse events, or AEs, were fatigue (8%), diarrhea (6%) and insomnia (6%). The most common adverse event was diarrhea, which was manageable and reversible. There was no evidence of the serious liver or common ocular toxicities seen with other Hsp90 inhibitors. This differentiated safety profile relative to other Hsp90 inhibitors is consistent with Phase 1 results and results from our other ongoing clinical trials with ganetespib, constituting over 350 patients treated to date.

This Phase 2 NSCLC trial of ganetespib is ongoing. Additional results from this trial are expected to be presented by mid-2011.

In addition to the Phase 2 NSCLC trial, two other company-sponsored clinical trials of ganetespib have been initiated to date: a Phase 1/2 clinical trial in hematologic cancers with a once-a-week dosing schedule and a Phase 2 clinical trial in GIST. While ganetespib showed some evidence of clinical activity in these trials, our near-term plans for company-sponsored trials are focused on advancing ganetespib in NSCLC. We are in discussions to continue development of ganetespib in GIST and hematologic cancers in investigator-sponsored or cooperative-group-sponsored trials.

In 2010, we also began collaborating with a number of clinical investigators to develop plans for testing ganetespib in specific tumor types in several different investigator-sponsored trials, or ISTs. An IST is a clinical trial conducted with an institution in which the principal investigator makes the regulatory filings and is responsible for the conduct of the trial, including adverse event reporting, data collection and analysis. ISTs typically enroll a relatively small number of patients and are limited to one or a few clinical sites. While we have less control over the conduct of ISTs compared to company sponsored trials, ISTs tend to be considerably less expensive than company sponsored clinical trials.

Eight ganetespib ISTs have been initiated to date, including Phase 2 trials in colorectal cancer, gastric cancer, small cell lung cancer, ocular melanoma, pancreatic cancer, prostate cancer, and breast cancer. In addition, a Phase 1/2 IST was initiated in hepatocellular (liver) cancer. We expect initial results from certain of these ISTs in the second half of 2011.

In January 2011, we announced that the MMRF will provide funding of up to \$1 million for a Phase 1 trial evaluating ganetespib as a single agent and in combination with Velcade for the treatment of relapsed multiple myeloma. We expect this trial to begin in the second half of 2011. We expect to initiate several additional ISTs in 2011 that will evaluate ganetespib in other tumor types or in combination with additional chemotherapy or targeted agents.

Many of the clinical and preclinical results described above were presented at recent scientific meetings including the 8th Annual International Symposium on Targeted Anticancer Therapies (March 2010), April 2010 AACR meeting, ASCO 2010, 11th International Lung Cancer Congress (July 2010), 22nd EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics (November 2010), the December 2010 ASH meeting, 33rd Annual San Antonio Breast Cancer Symposium (December 2010), and the 11th Annual Targeted Therapies of the Treatment of Lung Cancer meeting (February 2011).

### Future Plans for Ganetespib

Our future plans for ganetespib focus on advancing this drug candidate broadly along five dimensions:

- 1) As a monotherapy, in certain biomarker-defined patient populations
  - Certain specific gene mutational profiles have been associated with "Hsp90 addicted" cancers, in which treatment with ganetespib as a single agent has potential to produce pronounced, durable tumor regression.
- 2) In combination with taxanes, such as docetaxel and paclitaxel, in multiple tumor types in which taxanes are used

Preclinical evidence suggests pronounced synergy between the underlying anti-cancer effects of taxanes and Hsp90 inhibition. We believe that this synergy may be due to the ability of Hsp90 inhibition to sensitize cells to killing by taxanes, and to suppress certain mechanisms by which cells escape killing by taxanes.

3) In combination with certain tyrosine kinase inhibitors, angiogenesis inhibitors, and/or proteasome inhibitors

Certain compounds with these mechanisms have shown promising preclinical evidence of synergy in combination with ganetespib. These include compounds that inhibit VEGF, such as Avastin; compounds that inhibit EGFR, such as Tarceva or Iressa; compounds that inhibit the IGF1R, PI3K/mTOR/AKT pathway, such as Torisel; and compounds that act via proteasome inhibition, such as Velcade.

4) In breast cancer or prostate cancer, as a potential way to increase sensitivity to hormone receptor antagonist therapy and delay the time to treatment with chemotherapy

Because estrogen receptor and androgen receptor are client proteins of Hsp90, and because early stages of breast cancer and prostate cancer are believed to be due to aberrant signaling through these receptors, treatment with ganetespib may provide benefit in these earlier stages of breast cancer, before chemotherapy is used. Data presented at the San Antonio Breast Cancer Symposium in December 2010 showed that co-administration with ganetespib can restore sensitivity to and improve the anti-cancer activity of hormone receptor antagonist therapy in breast cancer.

- 5) As a means of sensitizing tumors to radiation therapy
  - Radiation therapy causes a rapid increase in stress inside cells and the unfolding and subsequent inactivation of proteins, leading to cell death. Hsp90 provides an important means by which cells repair protein unfolding and recover from this increased stress. By inhibiting Hsp90 function, we believe that ganetespib can suppress this repair mechanism. Preclinical experiments showed promising synergy of ganetespib in combination with radiotherapy.

#### Phase 2b/3 Trial in NSCLC

We are planning to initiate a Phase 2b/3 trial in NSCLC of ganetespib plus docetaxel versus docetaxel alone in the second quarter of 2011. This trial is being designed as a registration-enabling program with two stages. The first stage is an approximately 240 patient Phase 2b portion designed to establish the clinical benefit and safety profile of ganetespib in combination with docetaxel relative to docetaxel alone. This part of the trial will be used to build the clinical and operational experience needed to optimize the design of the second stage, Phase 3 portion of the trial. For example, we may use information obtained in the Phase 2b stage of the trial to refine patient inclusion/exclusion criteria to enrich the Phase 3 portion with those patients that show the greatest benefit from the addition of

ganetespib. The second stage, Phase 3 portion of the trial is expected to enroll between 400 to 600 patients.

We expect interim results from the first stage, Phase 2b portion of the trial by the end of 2011 or early 2012; with final results expected later in 2012. We expect interim results from the second stage, Phase 3 portion of the trial by the end of 2012 or early 2013; with final results expected later in 2013. We will discuss additional trial design details as the trial starts. an an an tha an a

#### Additional Hsp90 Inhibitors

We are currently developing a new series of Hsp90 inhibitor compounds that may be orally administered and may be more suitable for long-term treatment settings, such as adjuvant or maintenance therapy in oncology. We have also characterized additional small molecule, injectable Hsp90 inhibitors that provide options for future development. These compounds are in the lead optimization stage. ,· •

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### **Elesclomol** (Mitochondria-Targeting Agent)

Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death, or apoptosis, in cancer cells through a novel mechanism: disrupting cancer cell energy metabolism by selectively targeting the electron transport chain in cancer cell mitochondria.

#### Elesclomol's Mechanism of Action

Our preclinical data suggests that upon infusion, elesclomol binds copper in plasma, causing a structural change enabling its uptake through membranes and into cells. Elesclomol binds copper in a positively charged state called Cu(II). Once inside mitochondria, the elesclomol-Cu(II) complex interacts with the energy production mechanism of the cell, or the electron transport chain. This interaction reduces the copper from Cu(II) to Cu(I), resulting in a cascade of reduction-oxidation, or redox, reactions, that causes a rapid increase of oxidative stress, disruption of mitochondrial energy production, and ultimately, triggering of the mitochondrial apoptosis pathway. Although mitochondria generate energy for cells, they can induce apoptosis under certain conditions, such as high levels of oxidative stress. By increasing oxidative stress inside mitochondria and inducing apoptosis, we believe that elesclomol attacks cancer cells through a new mechanism that may provide a means to overcome resistance to traditional chemotherapy or targeted therapy. Elesclomol has shown potent cancer-cell killing activity against a broad range of cancers in vitro, and synergistic anti-cancer activity with paclitaxel and other agents in animal models of cancer.

## LDH: A Potential Predictive Biomarker for Elesclomol Activity

LDH is an enzyme that plays a key role in cancer cell energy metabolism. Under normal oxygen, or normoxic, conditions, energy in tumors is primarily generated by conversion of nutrients to adenosine triphosphate, or ATP, in the mitochondria, with oxygen as a key component of this process. Levels of LDH generally remain in the normal range in this state. Under low oxygen, or hypoxic, conditions, energy in tumors is primarily generated by glycolysis in the cytoplasm, and levels of LDH may increase. Accordingly, LDH can be used as a marker of mitochondrial activity, or tumor cell metabolic state.

Elesclomol has been shown to have potent anti-cancer activity in a broad range of cancer types under normoxic conditions in which LDH level is low to normal. Under hypoxic conditions, where LDH levels are elevated, elesclomol's ability to disrupt oxygen-mediated energy production has limited effect, and elesclomol loses anti-cancer activity. Accordingly, we believe that elevated LDH levels can serve as a predictive indicator of which patients are unlikely to benefit from treatment with elesclomol. Clinical observations have been consistent with the preclinical findings that elesclomol activity depends on metabolic state at the cellular level. In three randomized trials, in a total of over 800 patients, elesclomol showed clinical activity that correlated with baseline level of LDH. Benefit was seen only in patients with the low to normal levels of LDH associated with normoxic conditions.

The following chart summarizes the results of the three randomized, controlled, multi-center trials of elescional illustrating the differential response seen in high (LDH>1xULN) LDH patients versus low (LDH<0.8xULN) LDH patients:

	• • •	Elesciomol-Ph 3 melanoma Paclitaxel +/- elesciomol; 1:1 randomization*	lomol-Ph 3 elanoma itaxel +/- elsclomol; esclomol; 86 patients;		Elesciomol–Ph 2b melanoma Paclitaxel +/– elesciomol; 78 patients; 2:1 randomization	
		Median PFS (mo.)		Median PFS (mo.)	977	Median PFS (mo.)
	N	P+E vs. P	<u>N</u>	CP+E vs. CP	N	P+E vs. P
$LDH < 0.8x ULN \dots$	174	4.3 vs. 3.1	35	4.6 vs. 3.1	32	7.1 vs. 3.5
$LDH > 1x ULN \dots$	153	1.8 vs. 2.0	27	2.8 vs. 6.3	34	1.7 vs. 1.6

Phase 3 Melanoma trial: Data as of March 9, 2010 (ASCO 2010 presentation) for all patients enrolled as of November 1, 2008 (N=422 out of 651 total enrolled): those patients who had the opportunity to receive four cycles of treatment prior to February 25, 2009 study termination. LDH <1x or >1x was pre-specified stratification variable. Trial achieved primary PFS endpoint in the pre-specified LDH<1x population ITT analysis (p=0.036)

In our ongoing and planned studies with elesclomol, we anticipate enrolling only patients with low to normal LDH levels, as these are the patients we believe are most likely to derive benefit from treatment with elesclomol.

In clinical trials to date, the most common adverse events in the elesclomol plus paclitaxel groups included fatigue, alopecia, constipation, nausea, hypoaesthesia, arthralgia, insomnia, diarrhea, and anemia.

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, or 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, or 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, or NCI, is providing financial support of up to approximately \$300,000 for the trial through its Cancer Therapy Evaluation Program, or CTEP. In the second quarter of 2011, we plan to initiate a Phase 2b trial for elesclomol in NSCLC with a trial design similar to our prior Phase 2b trial for elesclomol in NSCLC. This new trial, which is expected to enroll approximately 180 patients, would prospectively specify that only patients with low to normal LDH levels will be enrolled. This trial will include a dose-escalation and safety portion to optimize the dose selection for the Phase 2b portion. We expect the randomized Phase 2b portion to begin in the fourth quarter of 2011.

#### 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. In animal models, STA-9584 has been shown to target both new and established tumor blood vessels, in contrast to the mechanism of action of angiogenesis inhibitors such as Avastin, which only prevent the formation of new tumor vasculature. STA-9584 has shown strong anti-tumor activity in a broad range of preclinical cancer models, including prostate, lung, breast, melanoma, and lymphoma. These models have shown that STA-9584 may kill tumor cells directly, in addition to disrupting established tumor blood vessels. This program is currently in preclinical development, with a focus in prostate cancer.

#### STA-9584's Mechanism of Action

STA-9584 is among a class of compounds known as Vascular Disrupting Agents, or VDAs. In preclinical models, STA-9584 efficiently kills both cancer cells in tumors as well as the endothelial cells that form blood vessels in tumors, without affecting the vasculature of non-tumor tissues. The inhibition of angiogenesis and disruption of existing tumor vasculature can prevent transport of oxygen and essential nutrients needed by tumors, and lead to substantial tumor shrinkage, particularly in bulky tumors that rely heavily on blood vessels for survival.

First generation angiogenesis inhibitors, such as Avastin, work primarily by preventing the formation of new tumor vessels. In contrast, STA-9584 disrupts both new and established tumor vessels. STA-9584's more complete anti-vasculature mechanism, together with complementary direct cancer-cell killing, have potential to be important advantages relative to first generation angiogenesis inhibitors and other endothelial cell-targeted agents.

#### STA-9584 Development Plans

In November 2010, we announced that the DoD recommended funding of STA-9584 for study in advanced prostate cancer. Under the DoD Prostate Cancer Research Program (PCRP) of the Office of the Congressionally Directed Medical Research Programs (CDMRP), STA-9584 was approved for a grant of approximately \$1 million. We anticipate initiating work supported by this grant during the first half of 2011.

#### Our Inflammatory Disease Programs

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

#### Inflammatory Disease Background

Inflammatory diseases are typically caused by aberrant activity of the immune system. The immune system normally protects the body from injury and infection, but in autoimmune diseases it attacks and damages the body's own tissues. Major autoimmune diseases include rheumatoid arthritis, or RA, psoriasis, Crohn's disease, and multiple sclerosis.

Despite the availability of numerous therapeutic options for these diseases, inflammatory diseases remain major causes of impairment of daily activities, reduced quality of life, significant disability, and sometimes death. Current therapeutic treatments for chronic inflammatory diseases have the potential to cause musculoskeletal, endocrine, neurologic, and metabolic side effects, which can limit their long-term use. The limitations of conventional treatments, together with a growing understanding of the pathogenesis of inflammatory diseases, have stimulated significant interest in the development of targeted immune modulators for the management of chronic inflammatory diseases.

#### **CRACM** Ion Channel Inhibitors

Ion channels, the gateways in cell membranes that regulate the flow of ions into and out of cells, play important roles in cell signaling. Certain ion channels allow electrically excitable cells, such as neurons or muscle cells, to discharge. Drugs that modulate these ion channels have proven to be a successful therapeutic category, with dozens of such drugs on the market and commonly prescribed for the treatment of various neurological and cardiovascular disorders. Our CRACM research program targets an ion channel that is believed to play a key role specifically in immune cells rather than in neurons or muscle cells. The CRACM ion channel is the primary route for calcium entry into T cells and other immune cells, regulating multiple immune cell processes important for initiating and maintaining an inflammatory immune response. CRACM channels regulate the calcium signaling pathway driving immune cell activation and secretion of TNFalpha, IL-2, and other inflammatory factors. The therapeutic importance of inhibiting this calcium signaling pathway has been demonstrated through clinical experience with calcineurin inhibitors, such as cyclosporine, which are potent immunomodulators but have significant toxicities due to the broad role calcineurin plays in nonimmune cells. In contrast to calcineurin, CRACM channels are believed to be critical exclusively to immune cell function. CRACM inhibitors therefore have the potential to achieve potent anti-inflammatory activity with an improved safety profile, creating the potential for a new category of disease-modifying agents comparable to biologic agents, such as TNF-alpha inhibitors, but orally available.

We have developed novel, small molecule inhibitors of CRACM ion channels expressed on immune cells. Our CRACM ion channel inhibitors have shown strong antiinflammatory 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 RA, asthma, chronic obstructive pulmonary disease, or COPD, allergy, transplant rejection, and other autoimmune diseases and inflammatory conditions. As part of our strategic alliance with Roche, Roche is advancing several compounds in preclinical development.

We also have several CRACM inhibitors that are not licensed to Roche in lead optimization. Because there are a number of CRACM ion channel targets on immune cells, we believe that our next generation CRACM inhibitor compounds could potentially apply to different immune system diseases and address distinct therapeutic areas, such as RA, allergy, asthma, and transplant rejection.

#### Roche CRACM Inhibitor Alliance

In December 2008, we formed a strategic alliance with Roche to discover, develop, and commercialize small-molecule drugs targeting CRACM channels. We refer herein to the agreement, as amended in February 2010 and February 2011, as the Roche Agreement. The goal of this alliance is to

develop a novel category of oral, disease-modifying agents for the treatment of rheumatoid arthritis and other autoimmune diseases and inflammatory conditions. Under the terms of the Roche Agreement, we received a \$16 million non-refundable upfront license fee. Roche funded research and development conducted by us in 2009 and 2010 and received worldwide rights to develop and commercialize certain products, referred to as Licensed Compounds, identified and studied prior to the end of the two-year research term, which concluded in December 2010. As of December 31, 2010, we received approximately \$21.1 million in research and development support from Roche. In the February 2011 amendment of the Roche Agreement, we extended the term of the research license for Roche to continue performing research on certain specified compounds until June 30, 2011. We are not performing any research on behalf of Roche and we will not receive any additional research and development support from Roche during the extended period of the research license. That amendment also provided for the return to us of certain Licensed Compounds. We retain all development and commercialization rights for our CRACM inhibitor compounds other than the specific Licensed Compounds licensed to Roche under the Roche Agreement. Roche is responsible for development and commercialization of the Licensed Compounds, while we retain certain co-development and co-promotion rights. We are also eligible to receive additional payments, for each of three Licensed Compounds, should specified development and commercialization milestones be successfully achieved. We will also receive tiered royalties on sales of all approved, marketed products containing Licensed Compounds.

#### 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, or 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 micro organisms, 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, or API, for our drug candidates. We also have the internal capability to synthesize small molecule compounds in quantities of up to several hundred grams 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, or 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, or cGMP, 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. At an appropriate time, we will discuss 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, or 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 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, with the exception of the CRACM ion channel program where we retain certain co-promotion rights with our partner Roche. 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 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 March 4, 2011, our patent portfolio had a total of 724 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 50 issued U.S. patents and 120 U.S. patent applications, as well as 554 foreign counterparts to these patents and patent applications.

With respect to our Hsp90 inhibitor program, we have 6 issued U.S. and foreign patents, and 104 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 drugs must be approved by the FDA through the new drug application, or NDA, process before they may be legally marketed in the United States.

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#### 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;
- license suspension or revocation;
- 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 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 the manufacturing facility or facilities at which the product is produced to assess compliance with current Good Manufacturing Practices, or cGMPs, to assure that the facilities, methods and controls are adequate to preserve the drug's 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 plan for any clinical trial before it commences at that institution. Each new clinical protocol must be submitted to the FDA as part of the IND. 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.* Involves studies 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 institutions for several reasons, including failure of 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 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 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 submission is accepted for filing, the FDA begins an in-depth 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. Before approving an NDA, the FDA will inspect the facility or facilities where the product is manufactured and tested.

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, we cannot be sure that the FDA will not later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will 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.

#### Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drugs, 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 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

Section 505(a) of the FDCA, as amended by the FDA Amendments Act of 2007, permits certain drugs to 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 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 requested or 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. 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. The FDA may not issue a Written Request for such studies or accept the reports of the studies.

#### 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, we 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 mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessments report each member state must decide whether to recognize approval. 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. If these 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 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. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, 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 often 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.

On February 17, 2009, President Obama signed into law the American Recovery and Reinvestment Act of 2009. This law 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 product 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 product candidates. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition.

The Patient Protection and Affordable Care Act and the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the Affordable Care Act or the ACA) enacted in March 2010, are expected to have a significant impact on the health care industry. 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, 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 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 ACA, as well as congressional efforts to repeal ACA, add to the uncertainty of the legislative changes enacted as part of ACA.

We expect that there will continue to be a number of federal and state proposals to implement governmental pricing controls and limit the growth of healthcare costs, including the cost of prescription drugs. At the present time, Medicare is prohibited from negotiating directly with pharmaceutical companies for drugs. However, Congress is currently considering passing legislation that would lift the ban on federal negotiations. In addition, Congress has been considering much broader regulation of healthcare and the House and Senate have passed different versions of bills for healthcare reform. While we cannot predict whether those bills will be reconciled or whether another version of healthcare reform legislation will be enacted into law, passage of such a law or the adoption of other legislative of regulatory proposals could have a material adverse effect on our business, financial condition and profitability.

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, 2010, we had 112 full time employees, including a total of 46 employees who hold M.D. or Ph.D. degrees. 82 of our employees are primarily engaged in research and development activities, and 30 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, SYMMETRY and the SYMMETRY logo. 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.

#### Item 1A. RISK FACTORS

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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, 2010, we had an accumulated deficit of \$351.1 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 and contemplated clinical trials of ganetespib in solid tumors and hematologic cancers and initiate additional clinical trials of ganetespib, including the planned initiation of a Phase 2b/3 clinical trial of ganetespib in combination with docetaxel in NSCLC, 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, including the planned initiation of a Phase 2b clinical trial of elesclomol in NSCLC, if supported by trial results;
- complete preclinical development of STA-9584 and initiate clinical trials, if supported by preclinical data;
- advance our CRACM inhibitor compounds not licensed to Roche under the Roche Agreement into preclinical development and initiate clinical trials, if supported by preclinical data;
- discover, develop, and seek regulatory approval for backups of our current drug candidates and other new drug candidates;
- identify additional compounds or drug candidates and acquire rights from third parties to those compounds or drug candidates through licenses, acquisitions or other means; and

• commercialize any approved drug candidates.

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

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.

#### 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 any additional clinical trials of ganetespib we may initiate in the future, including the planned initiation of a Phase 2b/3 clinical trial of ganetespib in combination with docetaxel in NSCLC, based on the results of these clinical trials;
- the results of preclinical studies of any additional Hsp90 inhibitors we may develop, and our decision to initiate clinical trials, if supported by preclinical data;
- the progress and results of our ongoing clinical trials of elesclomol and any additional clinical trials of elesclomol we may initiate in the future, including the planned initiation of a Phase 2b clinical trial of elesclomol in NSCLC, based on the results of these clinical trials;
- the results of our preclinical studies of STA-9584, and our decision to initiate clinical trials, if supported by the preclinical and other test results;
- the results of our preclinical studies of our CRACM inhibitor compounds not licensed to Roche under the Roche Agreement, and our decision to initiate clinical trials, if supported by the preclinical and other test results;
- Roche's ability to satisfy its obligations under the Roche Agreement, including payment of milestone and royalty payments;
- uncertainty associated with costs, timing, and outcome of regulatory review of our drug candidates;
- the scope, progress, results, and cost of preclinical development, clinical trials, and regulatory review of any new drug candidates we may discover or acquire;
- the costs of preparing, filing, and prosecuting patent applications and maintaining, enforcing, and defending intellectual property-related claims;

- our ability to establish additional strategic collaborations and licensing or other arrangements on terms favorable to us;
- the costs to satisfy our obligations under potential future collaborations; and
- the timing, receipt, and amount of sales or royalties, if any, from ganetespib, elesclomol, STA-9584, our CRACM inhibitors, our IL-12/23 inhibitors and our other potential products.

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

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

We do not anticipate that we will generate product revenue in the foreseeable future, if at all. We expect our continuing operations to use cash over the next several years and such cash use may increase significantly from year to year. While we are engaged in multiple preliminary partnership discussions for each of our currently unpartnered programs—ganetespib, elesclomol, STA-9584, CRACM compounds not licensed by Roche under the Roche Agreement, 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 2012. This estimate assumes that certain activities contemplated for 2011 will be conducted subject to the availability of sufficient financial resources. We are evaluating additional potential sources of funding, including partnership agreements, cost or risk-sharing arrangements, equity financings, use of our \$35 million equity line of credit facility or 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.

# 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 agreement contains affirmative and negative covenants that may restrict our business and financing activities. If we fail to comply with covenants in our loan and security agreement, 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.

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 inhibitor. 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.

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

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

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

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

### 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. 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 or delay the approval of ganetespib. While we have identified a possible improved formulation of ganetespib that we believe may broaden its commercial potential and decrease manufacturing risk, this new formulation has not yet been used in our clinical trials. If this formulation does not perform similarly compared with our current formulation of ganetespib, additional clinical trials may be required. Further, if this next generation 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. Although 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, there can be no assurances that we will continue the development of elesclomol in these indications, or 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. For example, in February 2009, we announced that we were suspending our Phase 3 SYMMETRY trial of elesclomol for the treatment of metastatic melanoma as well as all other ongoing studies of elesclomol. This decision to suspend the clinical development of elesclomol was based on the results of an interim analysis by the independent data monitoring committee, or DMC, of the SYMMETRY trial data. The DMC noted that while the primary endpoint of PFS showed a trend that favored the elesclomol plus paclitaxel, or ELPAC, arm of the study, early analysis of the secondary endpoint of overall survival, or OS, favored the control arm. Subsequently, elesclomol was put on clinical hold by the FDA at our request. 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 other clinical drug candidate, ganetespib, and our drug candidates that are still in preclinical studies, including STA-9584, our CRACM inhibitor candidate and our IL-12/23 inhibitor candidate:

- 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. Although in clinical trials to date, we have not observed the serious liver and common occular toxicities observed with first generation Hsp90 inhibitors, 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 the drug is safe and effective. In our completed Phase 2b clinical trial of elesclomol for metastatic melanoma, there were four patients with possible or probable drug-related serious adverse events related to treatment with elesclomol. In addition, in February 2009, we announced that we were suspending our Phase 3 SYMMETRY trial of elesclomol for the treatment of metastatic melanoma as well as all other ongoing studies of elesclomol. This decision to suspend the clinical development of elesclomol was based on the results of an analysis by the DMC of the SYMMETRY trial data. The DMC noted that while the primary endpoint of PFS showed a trend that favored the ELPAC arm of the study; early analysis of the secondary endpoint of OS favored the control arm. In an updated analysis presented at the American Society of Clinical Oncology in June 2010, we showed that baseline LDH levels were a predictive marker of treatment outcome in melanoma patients treated in the SYMMETRY trial. In patients with normal LDH levels, treatment with ELPAC showed improved PFS and neutral effect on OS, while in patients with elevated LDH levels, treatment with ELPAC showed no effect on PFS and a negative impact on OS.

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 clean up 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, medical institutions, and clinical investigators in the case of clinical trials, and contract research organizations 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 contract research organizations 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.

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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 manufactures 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 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 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 that has flexible scale manufacturing capabilities. We believe that the agreements we have entered into to date with these CMOs 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 preparation of the 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 our 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 they are unable to successfully increase the manufacturing capacity for a drug candidate, particularly elesclomol, 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 Roche does not develop and commercialize a licensed CRACM inhibitor compound on a timely basis, or at all, or if we are unable to partner our other CRACM inhibitors with another company on reasonable terms, or at all, we may be unable to develop and/or commercialize a CRACM inhibitor without additional capital.

In December 2008, we formed a strategic alliance with Roche to discover, develop, and commercialize small-molecule drugs targeting CRACM channels. We refer herein to the agreement, as amended in February 2010 and February 2011, as the Roche Agreement. Although the research collaboration phase of the Roche Agreement ended in December 2010, Roche remains responsible for development and commercialization of certain CRACM inhibitor compounds that were exclusively licensed to Roche under the Roche Agreement, or Licensed Compounds, while we retain certain co-development and co-promotion rights to the Licensed Compounds. We remain eligible to receive additional payments, for each of three Licensed Compounds, should specified development and commercialization milestones be successfully achieved by Roche. We will also receive tiered royalties on sales of all approved, marketed products containing Licensed Compounds. Other than the Licensed Compounds, we retain all worldwide rights to our CRACM inhibitor compounds and are free to develop such compounds alone or with another partner.

The Roche Agreement provides for certain termination provisions. Roche may terminate the agreement on a Licensed Compound-by-Licensed Compound basis upon providing advance written notice. Loss of Roche as a partner in the development or commercialization of the Licensed Compounds, any dispute over the terms of, or decisions regarding the agreement, or any other adverse developments in our relationship with Roche could result in an inability to develop and/or commercialize the Licensed Compounds.

We may not be successful in partnering our other CRACM inhibitors with another company on reasonable terms, or at all. The loss of Roche as a partner for the Licensed Compounds or our inability to successfully partner our other CRACM inhibitors with another company could accelerate our need for additional capital.

#### If we do not establish additional 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. In addition, because the research term under the Roche Agreement ended in December 2010, we are also solely responsible for future expenses related to the CRACM inhibitor compounds which are not covered under the development and commercialization license to Roche under the Roche Agreement. Our strategy also 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.

## 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.

#### **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.

As of March 4, 2011, our patent portfolio had a total of 724 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 50 issued U.S. patents and 120 U.S. patent applications, as well as 554 foreign counterparts to these patents and patent applications.

With respect to our Hsp90 inhibitor program, we have 6 issued U.S. and foreign patents, and 104 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 STA-9584, our CRACM ion channel inhibitors and our IL-12/23 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.

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 markets 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.

On February 17, 2009, President Obama signed into law the American Recovery and Reinvestment Act of 2009. This law 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 product 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 product candidates. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of the product candidate and have a material adverse effect on our sales, results of operations and financial condition.

In March 2010, the President signed the Patient Protection and Affordable Care Act and the Health Care and Education Affordability Reconciliation Act of 2010 (collectively, the Affordable Care Act or 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. For example, we may face product liability claims by patients treated with elesclomol, whether or not elesclomol harmed the patients in any way. 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 Division of Drug Marketing, Advertising, and Communications or other regulatory bodies.

The FDA's Division of Drug Marketing, Advertising, and Communications, or DDMAC, 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 DDMAC cite inadequate disclosure of risk information.

DDMAC 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 DDMAC 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, DDMAC 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 DDMAC, we may inadvertently violate DDMAC's guidelines in the future and be subject to a DDMAC untitled letter or warning letter, which may have a negative impact on our business. We are subject to federal and state laws prohibiting "kickbacks" and false or fraudulent claims, and state gift ban 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 antikickback law, and several 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. Other federal and state laws generally prohibit individuals or entities from knowingly presenting, or causing to be presented, claims for payment to Medicare, Medicaid or other third-party payors that are false or fraudulent, or for items or services that were not provided as claimed.

A number of states have enacted laws that require pharmaceutical and medical device companies to monitor and report payments, gifts and other remuneration made to physicians and other health care professional and health care organizations. 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. Similar legislation, known as the Physician Payments Sunshine Act, has been introduced in Congress each year for the past several years, but has not yet been enacted.

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 IPI-504 and IPI-493, being developed by Infinity Pharmaceuticals, AUY922 and HSP990, being developed by Novartis/Vernalis, KW-2478, being developed by Kyowa Hakko Kirin, MPC-3100, being developed by Myrexis, XL888, being developed by Exelixis, AT13387, being developed by Astex, and Debio0932, being developed by Curis/Debiopharma, among others.

*Elesclomol.* If approved, elesclomol may compete with other anticancer agents whose mechanisms may involve the induction of oxidative stress, including arsenic trioxide, hydroxyurea and NOV-002, being developed by Novelos/Mundipharma in the U.S. and marketed as Glutoxim by Pharma Vam in Russia.

*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 CA4P, being developed by Oxigene; AVE8062 being developed by Sanofi-Aventis, BNC105, being developed by Bionomics, MPC-6827 (Azixa), being developed by Myrexis, EPC-2407 (crolibulin), being developed by EpiCept, NPI-2358 (plinabulin) being developed by Nereus Pharmaceuticals, and CYT997, being developed by YM BioSciences.

*CRACM Ion Channel Inhibitors.* If approved, CRACM inhibitors may compete with the currently approved therapies for the treatment of inflammatory diseases, and other antiinflammatory 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.

All of our acquisitions to date have been of related parties. Accordingly, 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, 2010, 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;
- 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, executive officers and principal stockholders, together with their affiliates and related persons, beneficially own, in the aggregate, approximately 45% 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 2011
125 Hartwell Avenue Lexington, Massachusetts	27,060	Office and Laboratory	November 2011
45-47 Wiggins Avenue Bedford, Massachusetts	15,000	Office and Laboratory	October 2011

We are currently in negotiations to renew our expiring leases under our existing renewal options.

#### Item 3. LEGAL PROCEEDINGS

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

#### Item 4. (REMOVED AND RESERVED)

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#### 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.

<u>2009:</u>			· ·														High	Low	:
First Quarter	· • • • • •	••••				•••													
Second Quarte	r				•.•						 		••.				5.09	2.10	
Second Quarter . Third Quarter .				•••	•••	•••	••••	• • •		•••	 •	•••	• •	2 ·	<u>.</u>	<u>, 1</u>	3.33	2.11	: .
Fourth Quarter		•••	••••		•••		••	••	••	•••	 ••	•••	•.•	•••	•	•	6,95	2.59	
2010:			~				÷ -				.,	,			:		High	Low	
First Quarter																		\$3.81	
Second Quarter	r										 				• • •	• •	4.79	2.66	
Third Quarter					<i>.</i> .				<b>.</b> .		 · · .	• . •		•••		•••	4.13	2.55	
Fourth Quarter					•••						 		••		•••	•••	6.50	3.23	

#### Stockholders

As of March 4, 2011, there were approximately 93 stockholders of record of the 42,166,779 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.

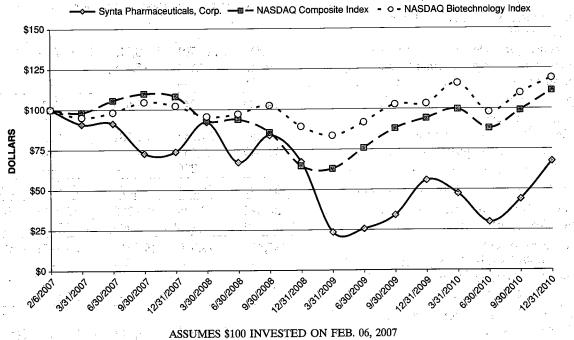
#### **Issuer Purchases of Equity Securities**

None.

#### Stock Performance Graph

The following graph compares the cumulative total stockholder return on our common stock from February 6, 2007 (the first trading date following our initial public offering) to December 31, 2010 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 February 6, 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 AMONG SYNTA PHARMACEUTICALS CORP., NASDAQ COMPOSITE INDEX AND NASDAQ BIOTECHNOLOGY INDEX



ASSUMES \$100 INVESTED ON FEB. 06, 2007 ASSUMES DIVIDEND REINVESTED FISCAL YEAR ENDING DEC. 31, 2010

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, 2010 and 2009, as well as consolidated statements of operations for the years ended December 31, 2010, 2009, and 2008, and the reports thereon are included elsewhere in this Annual Report on Form 10-K. The consolidated balance sheets as of December 31, 2008, 2007 and 2006, as well as the consolidated statements of operations for the years ended December 31, 2007 and 2006 are derived from our audited financial statements not included herein. 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,								
· · · · ·	2010	2009	2008	2007	2006				
	(all	(all amounts in thousands except per share data)							
<b>Consolidated Statement of Operations Data:</b>									
Revenues:				!!					
License and milestone revenue $(1)(2)$	\$ 4,572	\$125,701	\$ 8,513	\$ 743	\$				
Cost sharing reimbursements, net(1)(2) Grant revenue	9,253 978	18,544	(5,898)	· · · · · · · · · · · · · · · · · · ·	···				
Total revenues	14,803	144,245	2,615	743					
Research and development	40,252	51,054	81,581	52,025	50,503				
General and administrative	11,449	12,651	14,742	14,934	8,648				
Restructuring		1,236							
Total operating expenses	51,701	64,941	96,323	66,959	59,151				
Income (loss) from operations	(36,898) (569)	79,304 (216)	(93,708) 1,090	(66,216) 2,721	(59,151) 1,881				
Net income (loss)	(37,467)	79,088	(92,618)	(63,495)	(57,270)				
Convertible preferred stock dividends	. —		— —	· · ·	1,859				
Convertible preferred stock beneficial			· · · ·	50 505					
conversion feature	· · · · · · · · · · · · · · · · · · ·		. — —	58,585					
Net income (loss) attributable to common									
stockholders	<u>\$(37,467</u> )	\$ 79,088	<u>\$(92,618)</u>	\$(122,080)	<u>\$(59,129)</u>				
Net income (loss) attributable to common stockholders per share:	•								
Basic	\$ (0.93)		\$ (2.75)	\$ (3.76)	\$ (2.66)				
Diluted	\$ (0.93)	\$ 2.32	\$ (2.75)	\$ (3.76)	\$ (2.66)				
Basic	40,365	33,888	33,736	32,466	22,265				
Diluted	40,365	34,119	33,736	32,466	22,265				

•	As of December 31,										
	2010	2009	2008	2007	2006						
Consolidated Balance Sheet Data:				4							
Cash, cash equivalents and marketable securities	\$ 50,973	\$ 44,155	\$ 73,563	\$ 115,577	\$ 46,824						
Collaboration receivable(2)	116	·	16,000	<u> </u>							
Working capital	34,784	28,105	57,898	96,225	36,081						
Total assets	54,067	48,910	97,253	122,649	54,789						
Capital lease obligations, net of current portion	26	799	2,012	2,815	3,170						
Deferred collaboration revenue, net of			٤ •								
current portion(1)(2) $\ldots$	2,159	6,731	114,415	74,166	· · <u></u>						
Term loan, net of current portion	11,667	· · ·	·								
Convertible preferred stock	· · · · ·	· <u> </u>	<del></del>	·	41,820						
Common stock	. 4	3	3	3	2						
Additional paid-in capital	374,528	338,491	333,862	324,946	234,807						
Accumulated deficit	(351,050)	(313,583)	(392,671)	(300,053)	(236,558)						
Total stockholders' equity (deficit)	23,479	24,911	(58,791)	24,896	(1,747)						

 In October 2007, we entered into the GSK Agreement with GSK for elesclomol which was terminated in September 2009, resulting in immediate recognition of amounts previously deferred. See Notes 2 and 10 in the accompanying consolidated financial statements.

(2) In December 2008, we entered into the Roche Agreement with Roche for our CRACM inhibitor program. See Notes 2 and 9 in the accompanying consolidated financial statements.

## 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. Each of our drug candidates was discovered and developed internally using our proprietary, unique chemical compound library and integrated discovery engine. We have granted Hoffman-La Roche, or Roche, an exclusive license to develop and commercialize certain compounds from our calcium release activated calcium modulator, or CRACM, program resulting from our research partnership with them. We retain full ownership of all of our other drug candidates.

We believe that our competitive advantages include: the broad clinical and commercial potential of our drug candidates; the strength of our intellectual property portfolio, consisting of over 700 issued and pending patents; our proprietary chemical compound library and the strength of our drug discovery platform, with which we have generated all of our drug candidates; our ability to integrate discovery, translational, and clinical research to optimize our scientific and clinical choices and further strengthen our intellectual property position; our operational experience in effectively managing large-scale, global clinical programs; the full ownership of our programs, which creates strategic flexibility in partnership discussions that can be used to enhance the value we may ultimately capture from our drug candidates; our strong network of relationships with leading investigators and institutions, which facilitates our ability to conduct clinical trials efficiently; and the skills, talent, and level of industry experience of our employees. We believe that these competitive advantages provide us with multiple, sustainable growth opportunities.

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. We have funded our operations principally with \$311.7 million in net proceeds from private and public offerings of our common stock and Series A convertible preferred stock, including \$26.7 million in net proceeds from the sale of 6,388,889 shares of our common stock at \$4.50 per share in an underwritten public offering that was completed in January 2010 and \$5.0 million in net proceeds from the direct sale of 1,440,923 shares of our common stock at \$3.47 per share to a director and largest existing stockholder, that was completed in November 2010, as well as \$15.0 million in gross proceeds from a term loan that was executed in September 2010 with General Electric Capital Corporation, or GECC, and one other lender (referred to herein as the GECC Term Loan). In October 2010, we entered into a common share purchase agreement, or Purchase Agreement, with Azimuth Opportunity Ltd., or Azimuth, pursuant to which we obtained a committed equity line of credit facility, or Facility, under which we may sell up to a maximum of \$35 million or 8,106,329 shares of our common stock, whichever is fewer, over the 18-month term of the agreement, subject to certain conditions and limitations.

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, one of our oncology drug candidates, which we refer to as the GSK Agreement. On June 10, 2009, following the suspension of our global Phase 3 clinical trial of elesclomol plus paclitaxel in metastatic melanoma, called the SYMMETRY trial, we received written

notice from GSK of their intent to terminate the GSK Agreement. The collaboration terminated on September 10, 2009. In December 2008, as amended in February 2010 and February 2011, we entered into a collaborative license agreement with Roche, or the Roche Agreement, for our CRACM inhibitor program, which is currently in the preclinical stage. As of December 31, 2010, we have received \$167.1 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 \$21.1 million in research and development funding, which, together with the net cash proceeds from equity financings, the GECC Term Loan and the exercise of common stock warrants and options, provided aggregate net cash proceeds of approximately \$495.3 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, 2010, we had an accumulated deficit of \$351.1 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 (formerly STA-9090) is a potent, synthetic, small molecule inhibitor of Hsp90, a chaperone protein that is essential to the function of certain other proteins, for example tyrosine kinases that drive the growth, proliferation, and survival of many different types of cancer. Many of the known oncogenic proteins that play major roles in pathogenesis of solid tumor and hematologic malignancies are client proteins of Hsp90. By inhibiting Hsp90, ganetespib causes the degradation of these client proteins and the subsequent death of cancer cells dependent on these proteins. Ganetespib is structurally unrelated to the ansamycin family of first-generation Hsp90 inhibitors (such as 17-AAG and IPI-504) and has shown superior activity to these agents in preclinical studies. In clinical trials to date, ganetespib has shown encouraging evidence of clinical activity, including prolonged tumor shrinkage in patients who have progressed after, or failed to respond to, treatment with commonly-used drugs for these tumors. Currently, over 350 patients have been treated with ganetespib across all trials. Ganetespib has been well tolerated to date, with no evidence of the serious liver or common ocular toxicities seen with other Hsp90 inhibitors. The most common adverse event seen with ganetespib is diarrhea, which has been manageable and reversible with standard supportive care. Ganetespib is currently being evaluated in eleven Phase 2 clinical trials, with several additional trials expected to initiate in 2011, both as a single agent, or monotherapy, and in combination with other therapies.

In 2010, we initiated nine clinical trials, including a Phase 1 company-sponsored clinical trial of ganetespib in combination with docetaxel in solid tumors and eight investigator-sponsored trials, or ISTs, which include a Phase 1/2 trial in hepatic cancer and seven Phase 2 trials in colon, gastric, ocular melanoma, pancreatic, prostate, breast and small-cell lung cancers.

In January 2011, we announced that the Multiple Myeloma Research Foundation will provide funding of up to \$1 million for a Phase 1 trial evaluating ganetespib as a single agent and in combination with Velcade for the treatment of relapsed multiple myeloma. We expect this trial to begin in the second half of 2011. In addition, we expect to initiate several additional ISTs that will evaluate ganetespib in other tumor types or in combination with additional chemotherapy or targeted agents.

We are planning to initiate a Phase 2b/3 trial in NSCLC of ganetespib plus docetaxel versus docetaxel alone in the second quarter of 2011. This trial is being designed as a registration-enabling program with two stages. The first stage is an approximately 240 patient Phase 2b portion designed to establish the clinical benefit and safety profile of ganetespib in combination with docetaxel relative to docetaxel alone. This part of the trial is expected to require \$10 million or less in external costs in 2011. The first stage of this trial will be used to build the clinical and operational experience needed to optimize the design of the second stage, Phase 3 portion of the trial. For example, we may use information obtained in the Phase 2b stage of the trial to refine patient inclusion/exclusion criteria to enrich the Phase 3 portion with those patients that show the greatest benefit from the addition of ganetespib. The second stage, Phase 3 portion of the trial is expected to enroll between 400 to 600 patients.

We are currently developing a new series of Hsp90 inhibitor compounds that may be orally administered and may be more suitable for long-term treatment settings such as adjuvant or maintenance therapy in oncology. We have also characterized additional small molecule, injectable Hsp90 inhibitors that provide options for future development. These compounds are in the lead optimization stage.

#### Elesclomol (Mitochondria-Targeting Agent)

Elesclomol is a first-in-class, investigational drug candidate that triggers programmed cell death, or apoptosis, in cancer cells through a novel mechanism: disrupting cancer cell mitochondrial metabolism. Results from three randomized clinical trials and subsequent research have established that the patient baseline serum level of lactate dehydrogenase, or LDH, is an important predictor of elesclomol treatment outcome. Elesclomol is currently in a Phase 2 clinical trial in ovarian cancer in combination with paclitaxel and a Phase 1 clinical trial in acute myeloid leukemia, or AML, as a single agent.

In the second quarter of 2011, we plan to initiate a Phase 2b trial for elesclomol in NSCLC with a trial design similar to our prior Phase 2b trial for elesclomol in NSCLC. This new trial, which is expected to enroll approximately 180 patients, would prospectively specify that only patients with low to normal LDH levels will be enrolled. This trial will include a dose-escalation and safety portion to optimize the dose selection for the Phase 2b portion. We expect the randomized Phase 2b portion to begin in the fourth quarter of 2011.

#### GSK Elesclomol Alliance

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

#### 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 November 2010, we announced that the United States Department of Defense recommended funding of STA-9584, in the amount of approximately \$1 million, for study in advanced prostate cancer. We anticipate initiating work supported by this grant during the first half of 2011.

#### **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 antiinflammatory 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, or RA, asthma, chronic obstructive pulmonary disease, or COPD, allergy, transplant rejection, and other autoimmune diseases and inflammatory conditions. As part of our strategic alliance with Roche, Roche is advancing several compounds in preclinical development.

We have several CRACM inhibitors, which are not licensed to Roche, in lead optimization. Because there are a number of CRACM ion channel targets on immune cells, we believe that our next generation CRACM inhibitor compounds could potentially apply to different immune system diseases and address distinct therapeutic areas, such as RA, allergy, asthma, and transplant rejection.

#### Roche CRACM Inhibitor Alliance

In December 2008, we formed a strategic alliance with Roche to discover, develop, and commercialize small-molecule drugs targeting CRACM channels. We refer herein to the agreement, as amended in February 2010 and February 2011, as the Roche Agreement. The goal of this alliance is to develop a novel category of oral, disease-modifying agents for the treatment of RA and other autoimmune diseases and inflammatory conditions.

Under the terms of the Roche Agreement, we received a \$16 million non-refundable upfront license fee. Roche funded research and development conducted by us, which included discovery and certain early development activities. As of December 31, 2010, we have received approximately \$21.1 million in research and development support under the Roche Agreement. Roche received worldwide rights to develop and commercialize certain products, referred to as Licensed Compounds, which were identified and studied prior to the end of the two-year research term that concluded on December 31, 2010. We do not expect to earn any cost sharing revenue or receive any additional research and development support under the Roche Agreement in 2011. Roche is responsible for development and commercialization of the Licensed Compounds, while we retain certain co-development and co-promotion rights. We are also eligible to receive additional payments, for each of three Licensed Compounds, should specified development and commercialization milestones be successfully achieved. Development milestones across multiple indications of up to \$245 million could be earned for the first product, and up to half of this amount could be earned for each of the second and third products. Commercialization milestones of up to \$170 million could be earned for each of three products. We will also receive tiered royalties on sales of all approved, marketed products containing Licensed Compounds.

In the February 2011 amendment of the Roche Agreement, we extended the term of the research license for Roche to continue performing research on certain specified compounds until June 30, 2011.

That amendment also provided for the return to us of certain Licensed Compounds. We retain all development and commercialization rights for our CRACM inhibitor compounds other than the specific Licensed Compounds licensed to Roche under the Roche Agreement.

#### IL-12/23 Inhibitors

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

#### **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 have been generated primarily through partnership agreements with GSK and Roche. The terms of these agreements include 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. Upfront license payments and milestones are recognized ratably as collaboration revenue using the time-based model over the estimated performance period and any changes in the estimated performance period could result in substantial changes to the period over which these revenues are recognized (see "Critical Accounting Policies and Estimates—Revenue Recognition"). 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 the related 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 our stage of development. 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 and the expense of filing, prosecuting, defending or enforcing any patent claims or other intellectual property rights. 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 2011, we anticipate that our overall research and development expenses for personnel and external costs will increase as we further advance the clinical development of ganetespib and elesclomol. However, these increases will be offset in part due to the anticipated lower investment in CRACM research following the conclusion on December 31, 2010 of the initial two-year research term under the Roche Agreement.

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 2011, we anticipate our general and administrative expenses will remain at levels similar to 2010.

#### Restructuring

On March 12, 2009, we committed to a restructuring plan that consisted primarily of an immediate workforce reduction of approximately 90 positions, to a total of approximately 130 positions, to align our workforce to our revised operating plans following the suspension of our SYMMETRY clinical trial. In the first quarter of 2009, we recorded a restructuring charge of approximately \$1.2 million for severance and estimated benefits continuation costs and outplacement services. In addition, we paid approximately \$0.2 million in unused paid-time off that had been recognized as expense prior to the restructuring, including \$0.1 million in the year ended December 31, 2008 and \$0.1 million in the first quarter of 2009. The approximate \$1.4 million in restructuring related payments for severance, unused paid-time off, benefits and outplacement services was fully paid in 2009. To conserve additional capital

resources, we did not renew one of our office building leases that expired in August 2009 and consolidated our operations within our three other facilities. We did not incur an impairment charge in connection with the facility consolidation.

#### **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 contract research 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.

We believe the following accounting policies and estimates are most critical to aid in understanding and evaluating our reported financial results.

#### Marketable Securities

Marketable securities consist of investments in high-grade corporate obligations that are guaranteed by the United States government, 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 we will be required to sell the security before the recovery of its amortized cost basis. During the years ended December 31, 2010 and 2009, 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 income (loss), which is a separate component of stockholders' equity. The fair value of these securities is based on quoted market prices. Realized gains and losses are determined on the specific identification method. During the years ended December 31, 2010 and 2009, we recorded no realized gains or losses on marketable securities.

#### **Revenue** Recognition

#### Collaboration and License Agreements

Our principal source of revenue is from collaborative research and development agreements, which may include upfront license payments, development milestones, reimbursement of research and development costs, profit sharing payments, sales 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. We evaluate the multiple deliverables within our collaborations to determine whether the delivered elements that are our obligation have value to our collaborators on a stand-alone basis and whether objective reliable evidence of fair value of the undelivered items exists. Deliverables that meet these criteria are considered a separate unit of accounting. Deliverables that do not meet these criteria are combined and accounted for as a single unit of accounting. The appropriate recognition of revenue is then applied to each separate unit of accounting.

Our deliverables under our collaboration agreements, including the related rights and obligations, contractual cash flows and performance periods, are more fully described in Notes 8 and 9 of the accompanying consolidated financial statements. Certain of the deliverables have been combined as a single unit of accounting.

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

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. Sales 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, 2010, 2009 and 2008, 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, 2010, 2009 and 2008, respectively.

#### Stock-Based Compensation

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. Since we have a limited history of stock activity, expected volatility for the period from April 1, 2009 through December 31, 2010 was based upon the weightedaverage historical volatility data of our common stock and the 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. Prior to April 1, 2009, expected volatility was based solely on historical data from several similar guideline public biotechnology companies with similar stock compensation plans and terms. We will continue using our historical volatility and other similar public entity volatility information until our historical volatility alone is relevant to measure expected volatility for future option grants. We estimate the forfeiture rate based on historical data. Our options generally vest 25% after one year of service and quarterly over three years thereafter. Based on an analysis of historical forfeitures, we 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 interest 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. Accordingly, we amortize the fair value of each option over each option's service period, which is generally the vesting period.

We account for stock options issued to non-employees by valuing and remeasuring such stock options to the current fair value until the performance date has been reached.

Our net income (loss) included compensation costs in the amount of \$4.0 million, \$4.6 million and \$7.6 million for the years ended December 31, 2010, 2009 and 2008, respectively, and no income tax benefit related to our stock-based compensation arrangements for employee and non-employee awards. As of December 31, 2010, the total amount of unrecognized stock-based compensation expense was \$4.3 million, which will be recognized over a weighted average period of 1.8 years.

# **Consolidated Results of Operations**

# Years Ended December 31, 2010, 2009 and 2008

Revenue

			- 1				
		Years Ender December 31		2010 / 2 Compar		2009 / Compa	
	2010	2009	2008	\$	%	\$	%
			(dol	lars in millie	ons)		
Collaboration revenues:				1. A. 1	·		
License and milestone revenue—Roche	\$ 4.6	\$ 4.6	\$ 0.1	\$	%	\$ 4.5	4,500%
License and milestone revenue—GSK		121.1	8.4	(121.1)	<u>(100</u> )%	112.7	1,342%
	4.6	125.7	8.5	(121.1)	(96)%	117.2	1,379%
Cost sharing reimbursements, net—Roche	9.2	11.9		(2.7)	(23)%	11.9	%
Cost sharing reimbursements, net—GSK		6.6	(5.9)	(6.6)	<u>(100</u> )%	12.5	212%
	9.2	18.5	(5.9)	(9.3)	<u>(50</u> )%	24.4	414%
Total collaboration revenue	13.8	144.2	2.6	(130.4)	(90)%	141.6	5,446%
Grant revenue	1.0		r	1.0	—%		%
Total revenues	<u>\$14.8</u>	\$144.2	\$ 2.6	\$(129.4)	(90)%	\$141.6	5,446%

### Roche

*Overview* In December 2008, as amended in February 2010 and February 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 and, accordingly, we do not expect to earn any cost sharing revenue or receive any additional research and development support under the Roche Agreement in 2011. (See Notes 2 and 8 in the accompanying condensed consolidated financial statements.)

In 2010 as compared to 2009, cost sharing reimbursements from Roche decreased by \$2.7 million due to the realignment of our resources to focus on advancing the research program, thereby shifting preclinical and clinical development to Roche, as well as a corresponding lower level of research and development funding by Roche.

In 2009 as compared to 2008, we recognized a full year of license revenue in connection with the \$16 million nonrefundable upfront payment we received from Roche in January 2009 and we began performing research and development services under the Roche Agreement.

### GSK

*Overview:* In October 2007, as amended in June 2008, we entered into a collaborative development, commercialization and license agreement with GSK for elesclomol, received an \$80 million nonrefundable upfront payment from GSK and achieved a total of \$50 million in nonrefundable operational milestones. In 2008, we began recognizing, as a reduction to revenue, net cost sharing reimbursements due to GSK for costs they incurred under the development program. In 2009, following the suspension of the Company's global Phase 3 clinical trial of elesclomol plus paclitaxel in metastatic melanoma, called the SYMMETRY trial, GSK terminated the GSK Agreement effective September 10, 2009. (See Notes 2 and 9 in the accompanying condensed consolidated financial statements.)

In 2010 as compared to 2009, no revenue related to GSK was recognized due to the termination of the GSK Agreement in September 2009. In 2009 as compared to 2008, license and milestone revenue recognized under the GSK Agreement increased by \$112.7 million. In the third quarter of 2009, upon the effectiveness of the termination of the GSK Agreement, we recognized approximately \$114.6 million of remaining deferred revenue from upfront payments and milestones, all of which were recorded as license and milestone revenue as we had no further obligation for deliverables under the GSK Agreement to pay the cumulative GSK cost sharing reimbursements did not survive termination of the GSK Agreement and in the third quarter of 2009, upon the effectiveness of the termination of the GSK Agreement and in the third quarter of 2009, upon the effectiveness of the termination of the GSK Agreement, we reversed approximately \$10 million of cost sharing reimbursement liabilities as collaboration revenue.

#### Grant revenue

In 2010, we recognized grant revenue of \$1.0 million as compared to no grant revenue recognition in 2009. In November 2010, we were informed that all four Therapeutic Discovery Tax Credit applications we submitted under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or the Healthcare Reform Act of 2010, had been approved and that we had been awarded approximately \$1.0 million in grants. These funds were received in December 2010.

# Research and Development Expense

		ears Ende ecember 3		2010 / 2 Compar		2009 / 2 Compari	
$\hat{\mathbf{r}} = \hat{\mathbf{r}} + \mathbf{$	2010	2009	2008	\$	%	\$	%
$N_{\rm eff} = 2R_{\rm eff} + 2R_{$			(dolla	rs in millio	ons)		
Clinical-stage drug candidates Ganetespib Elesclomol Apilimod	2.9	\$14.7 19.7 0.5	\$ 6.3 60.1 <u>0.4</u>	\$ 11.3 (16.8) (0.5)	77% (85)% (100)%	\$ 8.4 (40.4) <u>0.1</u>	133% (67)% 25%
Total clinical-stage drug candidatesCRACMOther early stage programs	28.9 7.6 3.8	34.9 10.6 5.6	66.8 5.7 9.1	(6.0) (3.0) (1.8)	(17)% (28)% (32)%	(31.9) 4.9 (3.5)	(48)% 86% (38)%
Total research and development	\$40.3	<u>\$51.1</u>	\$81.6	\$(10.8)	(21)%	\$(30.5)	(37)%

#### Ganetespib

In 2010 as compared to 2009, costs incurred under our ganetespib program increased by \$11.3 million, principally including increases of \$6.6 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and \$4.7 million for external costs.

In 2009 as compared to 2008, costs incurred under our ganetespib program increased by \$8.4 million, principally including increases of \$6.9 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and \$1.5 million for external costs.

These increases in 2010 and 2009 were principally due to the advancement of clinical development, including fifteen ongoing clinical trials as of December 31, 2010, the manufacture of supporting drug supply, and the evaluation of additional cancer types and planning activities in connection with future clinical trials. In 2010, we initiated nine clinical trials, including a Phase 1 company-sponsored clinical trial of ganetespib in combination with docetaxel in solid tumors and eight investigator-sponsored clinical trials, which include a Phase 1/2 trial in hepatic cancer and seven Phase 2 trials in colon,

gastric, ocular melanoma, pancreatic, prostate, breast and small-cell lung cancers. In 2009, we initiated four company-sponsored clinical trials, including two Phase 1/2 clinical trials in hematologic cancers and two Phase 2 clinical trials in NSCLC and GIST. In 2011, we anticipate that the overall costs under our ganetespib program will continue to increase as we further advance clinical development, including the planned initiation of a randomized, registration-enabling Phase 2b/3 clinical trial of ganetespib in combination with docetaxel in NSCLC in the second quarter of 2011 and possible additional clinical trials in other cancer types, as well as the conduct of non-clinical supporting activities.

# Elesclomol

In 2010 as compared to 2009, costs incurred under our elesclomol program decreased by \$16.8 million, principally including decreases of \$7.5 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and \$9.3 million for external costs. These decreases were principally due to non-recurring costs incurred in 2009 resulting from the suspension of our previous elesclomol program and subsequent restructuring in the first quarter of 2009, offset in part by efforts in support of the restart of clinical development. In the fourth quarter of 2010, we initiated 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, with patient enrollment in these studies expected in the first quarter of 2011. In 2011, we anticipate that the overall costs under our elesclomol program will increase significantly as we further advance clinical development, including the planned initiation of a randomized Phase 2b clinical trial in NSCLC in the second quarter of 2011. This trial will include a dose-escalation and safety portion to optimize the dose selection for the Phase 2b portion. We expect the randomized Phase 2b portion to begin by the fourth quarter of 2011.

In 2009 as compared to 2008, costs incurred under our elesclomol program decreased by \$40.4 million, principally including decreases of \$12.3 million for personnel-related costs, related research supplies and operational overhead, \$2.9 million for stock compensation, and \$25.2 million for external costs. On February 26, 2009, we suspended the SYMMETRY trial, our global, pivotal Phase 3 clinical trial which was initiated in the third quarter of 2007, as well as the additional ongoing clinical studies using the sodium salt, water soluble formulation of elesclomol, including the Phase 1/2 trial of elesclomol in combination with docetaxel and prednisone in prostate cancer that was initiated in the fourth quarter of 2008 and the monotherapy Phase 1 trial in solid tumors that was initiated in January 2009. Subsequently, on March 12, 2009, we committed to a restructuring that consisted primarily of an immediate workforce reduction. In 2009, stock compensation decreased by \$2.9 million due in part to the workforce reduction in the first quarter of 2009 and in part to the non-recurring correction recognized in the first quarter of 2008. (See Note 2 in the accompanying condensed consolidated financial statements.)

#### Apilimod

In 2010 as compared to 2009, costs incurred under our apilimod program decreased by \$0.5 million principally due to decreases of \$0.2 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and \$0.3 million for external costs. Based on our review of the results of a Phase 2a clinical trial of apilimod in patients with RA, we do not expect to continue development of apilimod in this indication, with this formulation and route of administration. In 2009 as compared to 2008, costs incurred under our apilimod program principally increased by \$0.1 million due to a \$0.1 million increase for external costs.

### CRACM

In 2010 as compared to 2009, costs incurred under our CRACM program decreased by \$3.0 million, principally including decreases of \$2.0 million for personnel-related costs, related research

supplies, operational overhead and stock compensation, and \$1.0 million for external costs. These decreases reflect the realignment of our resources to focus on advancing the research program, thereby shifting preclinical and clinical development to Roche, as well as a corresponding lower level of research and development funding by Roche. In 2011, we anticipate that costs under the CRACM program will decrease as the result of a lower investment in CRACM research following the conclusion on December 31, 2010 of the initial two-year research term under the Roche Agreement.

In 2009 as compared to 2008, costs incurred under our CRACM program increased by \$4.9 million, principally including increases of \$4.1 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and \$0.8 million for external costs. The increase in external costs was principally due to the advancement of the program towards preclinical development.

#### Early-stage programs

In 2010 as compared to 2009, costs incurred under our other early-stage programs decreased by \$1.8 million principally due to decreases of \$1.2 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and \$0.6 million for external costs. In 2009 as compared to 2008, costs incurred under our other early-stage programs decreased by \$3.5 million principally due to decreases of \$3.1 million for personnel-related costs, related research supplies, operational overhead and stock compensation, and \$0.4 million for external costs.

General and Administrative Expense

		ears Ende ecember 3		2010 / : Compa		2009 / 3 Compa	
	2010	2009	2008	\$	%	\$	%
	·		(dollars	s in millio	ns)		<u>, a, </u>
General and administrative	\$11.4	\$12.6	\$14.7	\$(1.2)	(10)%	\$(2.1)	(14)%

In 2010 as compared to 2009, the decrease in general and administrative expense principally resulted from decreases of \$0.6 million for personnel-related costs and related overhead in connection with decreased headcount and stock compensation and \$0.6 million in external professional fees, including intellectual property and general legal fees, public-company reporting and compliance costs, director and officer insurance premiums, investor and medical-community relations, commercial development and corporate taxes. In 2011, we anticipate our general and administrative expenses will remain at levels similar to 2010.

In 2009 as compared to 2008, the decrease in general and administrative expense principally resulted from decreases of \$1.3 million for personnel-related costs and related overhead in connection with decreased headcount and stock compensation due in part to the workforce reduction in the first quarter of 2009 and \$0.8 million in external professional fees, including intellectual property and general legal fees, public-company reporting and compliance costs, director and officer insurance premiums, investor and medical-community relations, commercial development and corporate taxes.

#### Other (Expense) Income, net

		ears Ende ecember 3		2010 / Compa		2009 / Compa	
	2010	2009	2008	\$	%	\$	%
			(dolla	rs in mill	ions)		<u> </u>
Interest and investment income	\$	\$ 0.1	\$ 1.6	\$(0.1)	(100)%	\$(1.5)	(94)%
Interest expense	<u>(0.6</u> )	(0.3)	(0.5)	(0.3)	(100)%	0.2	40%
Other (expense) income, net	<u>\$(0.6</u> )	<u>\$(0.2</u> )	<u>\$ 1.1</u>	\$(0.4)	(200)%	\$(1.3)	(118)%

In 2010 as compared to 2009, interest and investment income decreased by \$0.1 million principally due to declining interest rates. Interest expense increased by \$0.3 million principally due to interest expense in connection with the GECC Term Loan that was executed in September 2010, offset by lower average principal balances of capital equipment leases. In 2011, we anticipate that interest expense will increase based upon a full year of interest expense related to the GECC Term Loan. In 2009 as compared to 2008, interest and investment income decreased by \$1.5 million principally due to declining interest rates and lower average cash balances, and interest expense decreased by \$0.2 million due to 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, 2010, 2009 and 2008.

	Year Er	ided Decem	ıber 31,	
	2010	2009	2008	
	(doll	ars in milli	ons)	
Cash, cash equivalents and marketable securities	\$ 51.0	\$ 44.2	\$ 73.6	
Working capital	34.8	28.1	57.9	, '
Cash flows (used in) provided by:				
Operating activities	(38.2)	(26.8)	(37.9)	
Investing activities	(19.8)	21.0	(23.7)	
Financing activities	45.2	(2.1)	(1.9)	
Capital expenditures (included in investing activities)	(0.1)	(0.5)	(2.2)	

Our operating activities used cash of \$38.2 million, \$26.8 million and \$37.9 million in 2010, 2009 and 2008, 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 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. In 2009, our investing activities provided cash of \$21.0 million, including maturities of marketable securities in our investment portfolio in the amount of \$60.8 million, offset by the purchases of marketable securities in the amount of \$39.3 million and purchases of property and equipment in the amount of \$0.5 million. In 2008, our investing activities used cash of \$23.7 million, including purchases of marketable securities in the amount of \$21.5 million and purchases of property and equipment in the amount of \$2.2 million.

Our financing activities provided cash of \$45.2 million in 2010, and used cash of \$2.1 million and \$1.9 million in 2009 and 2008, respectively. 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 and largest existing stockholder, as well as \$0.3 million from the exercise of common stock options. In 2008, we raised \$0.9 million in proceeds from the sale and lease-back of property and equipment. We repaid \$1.8 million, \$2.2 million and \$2.8 million in capital equipment leases in 2010, 2009 and 2008, respectively.

# Contractual Obligations and Commitments

The following tables summarize our contractual obligations at December 31, 2010 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, 2010)	Total	2011	2012 through 2013	2014 through 2015	More than 5 years
Capital lease obligations(1)	\$ 0.2	\$ 0.2	\$	\$—	\$ <u> </u>
Operating lease obligations		1.7	0.1		· _ · ·
Research and development contracts(2)	8.8	6.7	2.1	<u> </u>	
GECC Term Loan(1)	17.8	4.7	13.1		·
Total	\$28.6	<u>\$13.3</u>	\$15.3	<u>\$</u>	<u>\$</u>

(1) Including scheduled interest payments.

(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

We lease our research and office facilities under non-cancelable operating leases with terms expiring in 2011. We are currently in negotiations to renew our expiring leases under our existing renewal options. Each of these leases contains renewal options ranging from one to five years.

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 agreements, substantially all of which are related to our early-stage discovery programs, we may be obligated to pay up to an aggregate of \$1.5 million if specified development and commercialization milestones are met, as follows (in millions).

Milestone		Amount
Phase 1 clinical trials	•••	\$0.1
Phase 2 clinical trials		0.1
Phase 3 clinical trials	••	0.2
Completion of Phase 3 clinical trials	• •	0.1
FDA new drug approval	••	0.8
European market approval	••	_0.2
Total		\$1.5

# Term Loan with General Electric Capital Corporation (GECC)

On September 30, 2010, we entered into the \$15 million GECC Term Loan. Interest on the borrowings under the GECC Term Loan accrues at an annual rate of 9.75%. We will make interest-only payments through June 2011, followed by 27 equal monthly payments of principal plus accrued interest on the outstanding balance. In addition to the interest payable under the GECC Term Loan, we paid origination fees in the amount of \$150,000 and are obligated to pay an exit fee of \$450,000 at the time of the final payment of the outstanding principal. These amounts are being amortized and accreted, respectively, to interest expense over the term of the GECC Term Loan. We also paid approximately \$177,000 of legal fees and expenses in connection with the GECC Term Loan. These expenses have been deferred and, together with the \$150,000 origination fees, are included in other assets, and will be expensed over the term of the GECC Term Loan. In the year ended December 31, 2010, we recognized approximately \$453,000 in interest expense related to the GECC Term Loan. No warrants were issued in connection with the GECC Term Loan. We 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 our assets, except our intellectual property. We have granted GECC a springing security interest in our intellectual property in the event we are not in compliance with certain cash burn covenants, as defined. 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. We have determined that the risk of subjective acceleration under the material adverse events clause is remote. In addition, at the time of closing the GECC Term Loan, we were required to repay approximately \$787,000 of remaining principal outstanding under our existing equipment leases with GECC.

### Equity Line of Credit with Azimuth

On October 4, 2010, we entered into a common stock purchase agreement, or the Purchase Agreement, with Azimuth Opportunity Ltd., or Azimuth, pursuant to which we obtained an equity line of credit facility, which we refer to as the Facility, under which we may sell, in our sole discretion, and Azimuth is 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 our common stock, whichever is fewer, over the 18-month term of the agreement. Each draw down is limited in size, unless otherwise mutually agreed by the parties, to the lesser of (i) certain agreed-upon draw down amounts (the largest of which is \$4.25 million), based on the threshold price selected by us for the draw down, and (ii) 2.5% of our market capitalization at the time of such draw down. Azimuth is not required to purchase shares of our common stock if the threshold price is less than \$2.00 per share. The per share price of the shares sold in each draw down will be determined based on the daily volume weighted average price of our common stock on each trading day during the draw down period, less a discount ranging from 4.875% to 6%. The Purchase Agreement also provides that, from time to time and in our sole discretion, we may grant Azimuth the right to exercise one or more options to purchase additional shares of common stock during each draw down pricing period for the amount of shares based upon the maximum option dollar amount and the option threshold price specified by us. There were no transaction fees paid or warrants issued by us to Azimuth in connection with execution of the Purchase Agreement. Shares under the Facility, if issued, will be registered under our registration statement on Form S-3 declared effective by the Securities and Exchange Commission on August 28, 2008. Upon each sale of common stock to Azimuth, we will pay to Reedland Capital Partners a placement fee equal to 1.0% of the aggregate dollar amount received by us from such sale. To date, no shares have been sold to Azimuth under the Facility. The Purchase Agreement may be terminated by either party at any time.

# 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 and contemplated clinical trials of ganetespib in solid tumors and hematologic cancers and initiate additional clinical trials of ganetespib, including the planned initiation of a Phase 2b/3 clinical trial of ganetespib in combination with docetaxel in NSCLC, 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, including the planned initiation of a Phase 2b clinical trial of elesclomol in NSCLC, if supported by trial results;
- complete preclinical development of STA-9584 and initiate clinical trials, if supported by preclinical data;
- advance our CRACM inhibitor compounds not licensed to Roche under the Roche Agreement 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 any additional clinical trials of ganetespib we may initiate in the future, including the planned initiation of a Phase 2b/3 clinical trial of ganetespib in combination with docetaxel in NSCLC, based on the results of these clinical trials;
- the results of preclinical studies of any additional Hsp90 inhibitors we may develop, and our decision to initiate clinical trials, if supported by preclinical data;
- the progress and results of our ongoing clinical trials of elesclomol and any additional clinical trials of elesclomol we may initiate in the future, including the planned initiation of a Phase 2b clinical trial of elesclomol in NSCLC, based on the results of these clinical trials;
- the results of our preclinical studies of STA-9584, and our decision to initiate clinical trials, if supported by the preclinical and other test results;
- the results of our preclinical studies of our CRACM inhibitor compounds not licensed to Roche under the Roche Agreement, and our decision to initiate clinical trials, if supported by the preclinical and other test results;
- Roche's ability to satisfy its obligations under the Roche Agreement, including payment of milestone and royalty payments;
- 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, 2010, we had \$51 million in cash, cash equivalents and marketable securities, an increase of \$6.8 million from \$44.2 million as of December 31, 2009. This increase principally reflects \$47 million in net cash proceeds from financing activities and \$9.1 million in research and development funding from Roche, offset by cash used in operations as discussed under "Cash Flows" above. The \$47 million in net cash proceeds from financing activities includes \$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 million in net proceeds from the GECC Term Loan that was executed in September 2010 and \$5 million in net proceeds from the direct sale of 1,440,923 shares of our common stock in November 2010, as well as \$0.3 million from the exercise of common stock options.

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—ganetespib, elesclomol, STA-9584, CRACM compounds not licensed by Roche under the Roche Agreement, 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 2012. This estimate assumes that certain activities contemplated for 2011 will be conducted subject to the availability of sufficient financial resources. We are evaluating additional potential sources of funding, including partnership agreements, cost or risk-sharing arrangements, equity financings, use of our \$35 million equity line of credit facility 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, the credit markets and the financial services industry have recently been experiencing a period of turmoil and uncertainty that have made equity and debt financing more difficult to obtain. 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, including through offerings of securities pursuant to our shelf registration statement on Form S-3, under which we currently have up to \$116.2 million in securities available for issuance, including up to \$35.0 million in shares of common stock that we may offer and sell under the ELOC with Azimuth.

### **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

In 2005, 2007 and 2010, 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 for U.S. federal tax purposes of approximately \$288.6 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 2030 unless utilized. In addition, as of December 31, 2010, we have state net operating loss carryforwards of approximately \$160.4 million, which will expire through 2014 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.

#### **Recent Accounting Pronouncements**

Refer to Note 2, "Summary of Significant Accounting Polices," in the accompanying notes to the consolidated financial statements for a discussion of recent accounting pronouncements.

# 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, 2010, we had cash, cash equivalents and marketable securities of \$51 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 commercial paper and government-agency securities that are guaranteed by the U.S. government. 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, 2010, 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

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(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, 2010. 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, 2010, 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 Stockholders Synta Pharmaceuticals Corp.

We have audited Synta Pharmaceuticals Corp.'s. internal control over financial reporting as of December 31, 2010, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Synta Pharmaceuticals 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 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 Pharmaceuticals Corp. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2010, 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 as of December 31, 2010 and 2009, and the related consolidated statements of operations, stockholders' equity (deficit) and comprehensive income (loss) and cash flows for each of the three years in the period ended December 31, 2010 of Synta Pharmaceuticals Corp. and our report dated March 11, 2011 expressed an unqualified opinion riitud siiriitii siiriitii thereon. 9. E M

/s/ Ernst & Young LLP Boston, Massachusetts March 11, 2011

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(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. A substant of the state of the

# Item 9B. OTHER INFORMATION

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# 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 2011 Annual Meeting of Stockholders to be held on May 26, 2011.

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 2011 Annual Meeting of Stockholders to be held on May 26, 2011.

# 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 2011 Annual Meeting of Stockholders to be held on May 26, 2011.

# 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 2011 Annual Meeting of Stockholders to be held on May 26, 2011.

# Item 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Proposal No. 2—Independent Public Accountants" in our Proxy Statement for the 2011 Annual Meeting of Stockholders to be held on May 26, 2011.

# PART IV

Item 15.

Item 15(a)

Item 15(a)(1) and (2)

EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

The following documents are filed as part of this Annual Report on Form 10-K:

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

Exhibit Jumber	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
	reements	4 <u>- 1, 8</u>			e 14 4
10.1	Duffy Hartwell Limited Partnership Commercial Lease, dated November 4, 1996, by and between Duffy Hartwell Limited Partnership and Shionogi	ng na sa sa Ngga ng sa sa Ngga ng sa sa	S-1/A (Exhibit 10.5)	12/1/06	333-138894
· .	BioResearch Corp., as amended by First Amendment to Commercial Lease, dated August 30, 2006.	din e en al Algener Mat	en anter en la <del>s</del> la construction de la construcción la construcción de la construcción d		a Bata State and A
10.2	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
10.3	Lease of 125 Hartwell Avenue, Lexington, MA, dated October 26, 1992, by and between Fuji ImmunoPharmaceuticals Corp. and 125 Hartwell Trust, as amended by First Amendment dated January 31, 1993, Second Amendment dated October 1, 1997, Third Amendment dated November 1, 2002, Assignment and Assumption of Lease and Consent of Release by Landlord and Fourth Amendment of Lease, dated July 9, 2004, Fifth Amendment, dated October 22, 2004 and Sixth		S-1/A (Exhibit 10.6)	12/1/06	333-138894
10.4	Amendment, dated August 1, 2005. Seventh Amendment, dated November 26, 2007, to Lease of 125 Hartwell Avenue, Lexington, MA, dated October 26, 1992, by and between the Registrant, as successor-by-assignment, and 125 Hartwell Trust.		10-K (Exhibit 10.6.1)	3/20/08	001-33277
10.5	Eighth Amendment, dated June 19, 2008, to Lease of 125 Hartwell Avenue, Lexington, MA, dated October 26, 1992, by and between the Registrant, as successor-by-assignment, and 125 Hartwell Trust.		10-Q (Exhibit 10.2)	8/7/08	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	Ninth Amendment, dated May 19, 2009, to Lease of 125 Hartwell Avenue, Lexington, MA, dated October 26, 1992, by and between the Registrant, as successor-by-assignment, and 125 Hartwell Trust.		10-Q (Exhibit 10.1)	8/4/09	001-33277
10.7	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
10.8	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
Credit Fa	cilities and Loan Agreements				
10.9	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
	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
· ·	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.	X			

Exhibit	a tanàna 1990. Ara-ara-ara-ara-ara-ara-ara-ara-ara-ara-	Filed with this	Incorporated by Reference herein from Form or	Filing	SEC File / Registration
Number	Exhibit Description	Report	Schedule	Date	Number
10.12	Promissory Note issued by the Registrant to General Electric Capital Corporation.		8-K (Exhibit 10.1.2)	10/5/10	001-33277
10.13	Promissory Note issued by the Registrant to MidCap Funding III, LLC.	<i></i>	8-K (Exhibit 10.1.3)	10/5/10 -	001-33277
10.14	Guaranty, dated as of September 30, 2010, by and among Synta Securities Corp. and General Electric Capital Corporation.	· .	8-K (Exhibit 10.1.14)	10/5/10	001-33277
10.15	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
	nts with Respect to Collaborations, , Research and Development		in an		a <u>i</u>
†10.16	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
†10.17	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
†10.18 -	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
†10.19	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

Exhibit Number	Exhibit Description	Filed with this Report	Incorporated by Reference herein from Form or Schedule	Filing Date	SEC File / Registration Number
Equity (	Compensation Plans	·		· · · · · ·	
*10.20	2001 Stock Plan.		S-1/A (Exhibit 10.1)	12/1/06	333-138894
*10.21	Amended and Restated 2006 Stock Plan.		8-K (Exhibit 10.1)	6/21/10	001-33277
*10.22	Form of incentive stock option agreement under 2006 Stock Plan.		S-1/A (Exhibit 10.2(a))	1/23/07	333-138894
*10.23	Form of nonqualified stock option agreement under 2006 Stock Plan.		S-1/A (Exhibit 10.2(b))	1/23/07	333-138894
*10.24	Form of restricted stock agreement under 2006 Stock Plan.		S-1/A (Exhibit 10.2(c))	1/23/07	333-138894
*10.25	Form of nonqualified stock option agreement for directors under 2006 Stock Plan.		S-1/A (Exhibit 10.2(d))	1/23/07	333-138894
*10.26	Form of restricted stock agreement for directors under 2006 Stock Plan.		S-1/A (Exhibit 10.2(e))	1/23/07	333-138894
Agreeme	nts with Executive Officers and Directors			. •	
*10.27	Amended and Restated Director Compensation Policy, effective June 10, 2009.		10-Q (Exhibit 10.2)	8/4/09	001-33277
*10.28	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
*10.29	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
*10.30	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
*10.31	Letter Agreement, dated April 15, 2004, by and between the Registrant and Dr. Jeremy Chadwick.		S-1/A (Exhibit 10.16)	12/1/06	333-138894
*10.32	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
*10.33	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

Exhibit	in a statistica de la companya de la Companya de la companya de la company Companya de la companya de la company	Filed with this	Incorporated by Reference herein from Form or	Filing	SEC File / Registration Number
Number	Exhibit Description	Report	Schedule	<u> </u>	
*10.34	Letter Agreement, dated July 9, 2008, by and between the Registrant and Michael P. Bailey.		10-Q (Exhibit 10.12)	11/13/08	001-33277
*10.35	Letter Agreement, dated December 9, 2008, by and between the Registrant and Vojo Vukovic.		10-K (Exhibit 10.29)	3/11/10	001-33277
*10.36	Letter Agreement, dated November 19, 2010, by and between the Registrant and Amar Singh.	X			
*10.37	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
*10.38	Form of Severance and Change in Control Agreement between the Registrant and each of Keith S. Ehrlich and Wendy E. Rieder.	۰. ۲:	10-K (Exhibit 10.31)	3/11/10	001-33277
*10.39	Retention Award from the Registrant to Keith S. Ehrlich, dated April 14, 2009.		10-Q (Exhibit 10.3)	8/4/09	001-33277
*10.40	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
*10.41	Consulting Agreement, dated April 18 2005, by and between the Registrant and Lan Bo Chen, Ph.D.	3,	S-1/A (Exhibit 10.23)	12/1/06	333-138894
*10.42	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
*10.43	Form of Indemnification Agreement between the Registrant and its directors and executive officers.		S-1/A (Exhibit 10.26)	12/1/06	333-138894
*10.44	Summary of bonus arrangements applicable to the Registrant's Named Executive Officers.		10-K (Exhibit 10.23)	3/20/08	001-33277
10.45	Subscription Agreement, dated November 10, 2010, by and between the Registrant and Bruce Kovner.		8-K (Exhibit 10.1)	11/12/10	001-33277
21.1	List of Subsidiaries.		10-K (Exhibit 21.1)	3/28/07	001-33277

Exhibit Number		Exhibit Descript	tion	Filed with this Report	Incorporat Reference from For Schedu	herein m or	Filing Date	Regist	File / ration nber
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### 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 11, 2011

By: /s/ SAFI R. BAHCALL, PH.D.

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, PH.D. Safi R. Bahcall, Ph.D.	President, Chief Executive Officer and Director (principal executive officer)	March 11, 2011
		. (A. 1997) . (A. 1997)
/s/ KEITH S. EHRLICH Keith S. Ehrlich	Vice President, Finance and Administration, Chief Financial Officer (principal accounting and financial officer)	March 11, 2011
/s/ KEITH R. GOLLUST Keith R. Gollust	Chairman of the Board	March 11, 2011
/s/ LAN BO CHEN Lan Bo Chen, Ph.D	Director	March 11, 2011
/s/ BRUCE KOVNER Bruce Kovner	Director	March 11, 2011
/s/ DONALD W. KUFE Donald W. Kufe, M.D.	Director	March 11, 2011
/s/ WILLIAM REARDON William Reardon, C.P.A.	Director	March 11, 2011
/s/ ROBERT WILSON Robert N. Wilson	Director	March 11, 2011

# INDEX TO CONSOLIDATED FINANCIAL STATEMENTS SYNTA PHARMACEUTICALS CORP. Years ended December 31, 2010, 2009, and 2008

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#### **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, 2010 and 2009, and the related consolidated statements of operations, stockholders' equity (deficit) and comprehensive income (loss) and cash flows for each of the three years in the period ended December 31, 2010. 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, 2010 and 2009, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2010, 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, 2010, 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 11, 2011, expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts March 11, 2011

# **Consolidated Balance Sheets**

# (in thousands, except share and per share amounts)

	Decem	ber 31,
	2010	2009
Assets		
Current assets:		te will t
Cash and cash equivalents	\$ 31,310	\$ 44,155
Marketable securities	19,663	· · · <u> </u>
Collaboration receivable	116	
Prepaid expenses and other current assets	431	419
Total current assets	51,520	44,574
Property and equipment, net	2,181	3,978
Other assets	366	358
Total assets	\$ 54,067	\$ 48,910
Liabilities and Stockholders' Equity	· · ·	
Current liabilities:	ф <u>100</u> 7	* <u> </u>
Accounts payable	\$ 1,925	\$ 3,957
Other accrued liabilities	2,511 4,194	2,099 4,504
Capital lease obligations	4,194	4,304
Deferred collaboration revenue.	4,572	4,647
Term loan	3,333	
Total current liabilities	16,736	16,469
Long-term liabilities:		
Capital lease obligations	26	799
Deferred collaboration revenue	2,159	6,731
Term loan	11,667	
Total long-term liabilities	13,852	7,530
Total liabilities	30,588	23,999
Commitments and contingencies (Note 12)		
Stockholders' equity:		
Preferred stock, par value \$0.0001 per share Authorized: 5,000,000 shares at		
December 31, 2010 and 2009; no shares issued and outstanding at		
December 31, 2010 and 2009	_	. —
Common stock, par value \$0.0001 per share Authorized: 100,000,000 shares		
at December 31, 2010 and 2009; 42,090,205 and 33,978,300 shares issued and outstanding at December 31, 2010 and 2009, respectively	4	3
Additional paid-in-capital	374,528	338,491
Accumulated other comprehensive income	(3)	
Accumulated deficit	(351,050)	(313,583)
Total stockholders' equity	23,479	24,911
Total liabilities and stockholders' equity	\$ 54,067	\$ 48,910

See accompanying notes to consolidated financial statements.

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# **Consolidated Statements of Operations**

# (in thousands, except share and per share amounts)

	Years Ended December 31,				
	2010	2009	2008		
Revenues:					
Collaboration revenues:		•			
License and milestone revenue	\$ 4,572	\$ 125,701	\$ 8,513		
Cost sharing reimbursements, net	9,253	18,544	(5,898)		
Total collaboration revenues	13,825	144,245	2,615		
Grant revenue	978				
Total revenues	14,803	144,245	2,615		
Operating expenses:			an an an an Araba. Taona an Araba		
Research and development	40,252	51,054	81,581		
General and administrative	11,449	12,651	14,742		
Restructuring		<u> </u>	· · · · · · · · · · · · · · · · · · ·		
Total operating expenses	51,701	64,941	96,323		
Income (loss) from operations	(36,898)	79,304	(93,708)		
Other (expense) income, net	(569)	(216)	1,090		
Net income (loss)	\$ (37,467)	\$ 79,088	\$ (92,618)		
Net income (loss) per common share:	D				
Basic	\$ (0.93)	\$ 2.33	\$ (2.75)		
Diluted	\$ (0.93)		\$ (2.75)		
Weighted-average common shares outstanding:		,	a qui i		
Basic	40,365,215	33,887,766	33,735,579		
Diluted	40,365,215	34,118,846	33,735,579		
	· · ·		4		
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See accompanying notes to consolidated financial statements.

# Consolidated Statements of Stockholders' Equity (Deficit) and Comprehensive Income (Loss) (in thousands, except share amounts)

	Соттоп	stock	Additional paid-in	Accumulated other comprehensive	Accumulated	Total stockholders'	Comprehensive
· · ·	Shares	Amount		income (loss)	deficit	equity (deficit)	income (loss)
Balance at December 31, 2007	33,875,942	\$ 3	\$324,946	_	\$(300,053)	\$ 24,896	\$(63,497)
Issuance of restricted common			•	· · · · .			$C \in \overline{[1, 2^{n}, 2^{n}, 2^{n}]}$
shares	• 45,242	_		—		11 L	
Exercise of stock options Forfeitures of restricted	625		1	—	— .	1 .	•
common shares	(2,225)		_	· · · ·	·		.*
Compensation expense related							
to stock options for services .	·	—	7,572	· — ·	· · · · ·	7,065	
Reclassification of vested stock							at pol
options granted to				1	1. A. A.	19 11 11 11 11 11 11 11 11 11 11 11 11 1	
non-employee consultants Unrealized gain on marketable	_	—	1,343		_	1,850	
securities	_		<del></del>	15		15	15
Net loss	—		_	· _ · ·	(92,618)	(92,618)	(92,618)
Balance at December 31, 2008	33,919,584	3	333,862	15	(392,671)	(58,791)	(92,603)
Issuance of restricted common						· · · .	n in the second s
shares	46,216		· —	_		—	
Exercise of stock options	25,000		50	'	. —	50	19 1 1 N
Forfeitures of restricted					1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	i di s	
common shares	(12,500)		—				
Compensation expense related				· · ·			tan Sta
to stock options for services .	—		4,579		·	4,579	
Unrealized loss on marketable				(15)		(15)	115)
securities	. —		. —	(15)	70.022	(15)	(15)
Net income			·		79,088	79,088	79,088
Balance at December 31, 2009	33,978,300	<u>\$ 3</u>	\$338,491	<u>\$ —</u>	<u>\$(313,583)</u>	\$ 24,911	<u>\$ 79,073</u>
Issuance of common shares in	< <b>*</b> * * * * * * * * * * * * * * * * * *					0.000	
equity offering, net	6,388,889	1	26,688	<u> </u>	·	26,689	
Issuance of common shares to	1 440 000		4.007	۰.		4.095	
a related party, net	1,440,923	· .	4,985	— ·		4,985	a an
Issuance of restricted common	190 710		÷		1 A.	1. j. 1.	
shares	180,719	_	316	_		316	· · · · ·
Exercise of stock options Forfeitures of restricted	. 152,745		510			510	
common shares	(31,371)				· ·	·	
Compensation expense related	(31,371)			1 2 1	i in in		
to stock options for services		_	4,048	s	_	4,048	4 * j
Unrealized loss on marketable			1,040			.,	· · ·
securities	···		_	(3)	· · · · ·	(3)	(3)
Net loss		_	_	·	(37,467)	(37,467)	(37,467)
		<u></u>	\$374,528	\$ (3)	\$(351,050)	\$ 23,479	\$(37,470)
Balance at December 31, 2010		φ4 	φJ14,J20 	φ <u>(</u> 3)	φ(331,030) 	Ψ 43,477	
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See accompanying notes to consolidated financial statements.

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# **Consolidated Statements of Cash Flows**

# (in thousands)

	Years Ended December 3		er 31.
	2010	2009	2008
Cash flows from operating activities:			
Net income (loss)	\$(37,467)	\$ 79.088	\$(92,618)
Adjustments to reconcile net income (loss) to net cash used in		,	+ (, )
operating activities:			
Stock-based compensation expense	4,048	4,579	7,572
Depreciation and amortization	1,933	2,463	2,717
Changes in operating assets and liabilities:			
Collaboration receivable	(116)	16,000	. —
Restricted cash		151	(68)
Prepaid expenses and other current assets	(12)	1,088	(170)
Other assets	(8)	(255)	(27)
Accounts payable	(2,032)	626	840
Accrued contract research costs	412	(10,294)	8,876
Other accrued liabilities	(310)	1,663	(2,841)
Deferred collaboration revenue	(4,647)	(115,625)	31,486
Collaboration payable		(6,294)	6,294
Net cash used in operating activities	(38,199)	(26,810)	(37,939
Cash flows from investing activities:			
Purchases of marketable securities	(36,916)	(39,303)	(21,503)
Maturities of marketable securities	17,250	60,806	<del>.</del>
Purchases of property and equipment	(136)	(454)	(2,184
Net cash (used in) provided by investing activities	(19,802)	21,049	(23,687
Cash flows from financing activities:			
Proceeds from issuances of common stock and exercise of common			1.54
stock options, net of transaction costs	27,005	50	1
Proceeds from the sale of common stock to a related party	4,985		:
Proceeds from term loan	15,000		<u> </u>
Proceeds from sale—leaseback of property and equipment		·	880
Payment of capital lease obligations	(1,834)	(2,179)	(2,787
Net cash provided by (used in) financing activities	45,156	(2,129)	(1,906
Net decrease in cash and cash equivalents	(12,845)	(7,890)	(63,532
Cash and cash equivalents at beginning of period	44,155	52,045	115,577
Cash and cash equivalents at end of period	<u>\$ 31,310</u>	\$ 44,155	\$ 52,045
Supplemental disclosure of noncash operating, investing and			
financing activities:		•	· · · · ·
Collaboration receivable for upfront license payment	·		\$ 16,000
Acquisition of equipment under capital leases	_	\$ 58	\$ 1,748
Supplemental disclosure of cash flow information:			
Cash paid for interest	\$ 578	\$ 312	\$ 489

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 (FDA) and other government regulations.

The Company has incurred significant operating losses since its inception and, as a result, at December 31, 2010 had an accumulated deficit of \$351.1 million. Operations have been funded principally through the sale of common stock and convertible preferred stock, capital leases, non-refundable partnership payments under the agreements with GlaxoSmithKline (GSK) and Hoffman-La Roche (Roche), and proceeds from a term loan by General Electric Capital Corporation (GECC) (see Note 12). At December 31, 2010, the Company had approximately \$51.0 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 2012. This estimate assumes that certain activities contemplated for 2011 will be conducted subject to the availability of sufficient financial resources. The Company is evaluating additional potential sources of funding, including partnership agreements, cost or risk-sharing agreements, equity financings, use of its \$35 million equity line of credit facility (see Note 5) or other sources.

However, 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 accounting principles generally accepted in the United States (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 are recorded in the period in which they become known. Actual results could differ from those estimates.

### Notes to Consolidated Financial Statements (Continued)

# (2) Summary of Significant Accounting Policies (Continued)

### **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 U.S. Treasury 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

16 March 19 March 19

Marketable securities consist of investments in high-grade corporate obligations that are guaranteed by the United States government, 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, 2010 and 2009, 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 market prices. Realized gains and losses are determined on the specific identification method. During the years ended December 31, 2010 and 2009, 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 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—inputs other than Level 1 inputs that are either directly or indirectly observable, such as quoted market prices, interest rates and yield curves.

### Notes to Consolidated Financial Statements (Continued)

### (2) Summary of Significant Accounting Policies (Continued)

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. As of December 31, 2010, the Company's financial assets valued based on Level 1 inputs consisted of cash and cash equivalents in a U.S. Treasury money market fund and its financial assets valued based on Level 2 inputs consisted of corporate, government and government-agency bonds that are guaranteed by the U.S. government. As of December 31, 2010, the Company had no financial liabilities that were subject to fair value measurement.

### **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 approximately \$1.9 million, \$2.2 million, and \$1.9 million for the years ended December 31, 2010, 2009 and 2008, 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, 2010, 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 2007 through 2010 remain open to examination by the major taxing jurisdictions to which the Company is subject.

# Notes to Consolidated Financial Statements (Continued)

### (2) Summary of Significant Accounting Policies (Continued)

# 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, 2010 and 2009.

### **Revenue Recognition**

### **Collaboration and License Agreements**

The Company's principal source of revenue is from collaborative research and development agreements, which may include upfront license payments, development milestones, reimbursement of research and development costs, profit sharing payments, sales 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.

The Company evaluates the multiple deliverables within its collaborations to determine whether the delivered elements that are the obligation of the Company have value to its collaborators on a stand-alone basis and whether objective reliable evidence of fair value of the undelivered items exists. Deliverables that meet these criteria are considered a separate unit of accounting. Deliverables that do not meet these criteria are combined and accounted for as a single unit of accounting. The appropriate recognition of revenue is then applied to each separate unit of accounting.

The Company's deliverables under its collaboration agreements, including the related rights and obligations, contractual cash flows and performance periods, are more fully described in Notes 8 and 9. Certain of the deliverables have been 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 are recognized as revenue using a time-based model. Under this model, cash flow streams are recognized as revenue over the estimated performance period. Upon achievement of milestones, as defined in the collaboration agreements, revenue is recognized to the extent the accumulated service time, if any, has occurred. The remainder is deferred and recognized as revenue ratably over the remaining estimated performance period. A change in the period of time expected to complete the deliverable is accounted for as a change in estimate on a prospective basis. Revenue is limited to amounts that are non-refundable and that the Company's collaborators are contractually obligated to pay to the Company.

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. Sales 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.

### Notes to Consolidated Financial Statements (Continued)

# (2) Summary of Significant Accounting Policies (Continued)

# Grant Revenue

In November 2010, the Company was informed that all four Therapeutic Discovery Tax Credit applications it submitted under the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or the Healthcare Reform Act of 2010, had been approved and that the Company had been awarded approximately \$1.0 million in grants. These funds were received in December 2010 and have been recorded as grant revenue in the accompanying statement of operations.

### **Deferred** Collaboration Revenue

Consistent with the Company's policy on revenue recognition, deferred collaboration revenue represents cash received and amounts earned and invoiced for licensing and option fees and milestones, as well as cash received and amounts invoiced for research and development services to be performed by the Company. Such amounts are reflected as deferred collaboration revenue until revenue can be recognized under the Company's revenue recognition policy. Deferred collaboration revenue is classified as current if management believes the Company will complete the earnings process and be able to recognize the deferred amount as revenue within 12 months of the balance sheet date. At December 31, 2010, total deferred collaboration revenue was approximately \$6.7 million, of which \$4.6 million is current.

### 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. Since the Company has a limited history of stock activity, expected volatility for the period from April 1, 2009 through December 31, 2010 was 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. Prior to April 1, 2009, expected volatility was based solely on historical data from several guideline similar public biotechnology companies with similar stock compensation plans and terms. The Company will continue using its historical volatility and other similar public entity volatility information until its historical volatility alone is relevant to measure expected volatility for future option grants. 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.

# Notes to Consolidated Financial Statements (Continued)

### (2) Summary of Significant Accounting Policies (Continued)

The Company accounts for stock options issued to non-employees by valuing and remeasuring such stock options to the current fair value until the performance date has been reached.

For the years ended December 31, 2010, 2009 and 2008, the fair value of each employee stock option award was estimated on the date 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,			
	2010	2009	2008	
Risk-free interest rate	2.62%	2.05%	3.21%	
Expected life in years	6.25 years	5.78 years	6.25 years	
Volatility	102%	95%	70%	
Expected dividend yield	· · · · · ·		na dis <del>T</del> ribus S	

As part of its preparation of its quarterly financial statements for the three months ended March 31, 2008, the Company discovered that it had erroneously accounted for certain of its non-employee stock options during the last three quarters of 2007 as liabilities. Under this accounting it had reclassified approximately \$1.9 million from additional-paid-in capital to liabilities in the second quarter of 2007 and subsequently during the year adjusted the fair value of the liability for changes in the market price of its common stock, resulting in a \$553,000 credit to stock-based compensation expense for the year. The Company assessed the materiality of this error on its financial statements for the year ended December 31, 2007, using both the roll-over method and iron-curtain method. The Company concluded the effect of this error was not material to its financial statements for the year ended December 31, 2007 and, as such, these financial statements are not materially misstated. The Company also concluded that providing for the correction of the error in 2008 would not have a material effect on its financial statements for the year ended December 31, 2008. Accordingly, the Company recorded a charge to stock-based compensation of \$553,000 and a reclassification of approximately \$1.9 million from liabilities to additional-paid-in-capital in the three months ended March 31, 2008 to correct this error.

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# Notes to Consolidated Financial Statements (Continued)

### (2) Summary of Significant Accounting Policies (Continued)

The effect of stock-based compensation expense during the years ended December 31, 2010, 2009 and 2008 was as follows (in thousands):

	Years e	Years ended December 31	
	2010	2009	2008
Stock-based compensation expense by type of award:	• .	;	
Employee stock options	\$3,614	\$4,471	\$5,279
Repriced employee stock options			169
Employee options issued below fair value	, <del></del>	—	. 8
Non-employee stock options	· · · · <del></del>	17	588
Restricted stock:		91	1,528
Total stock-based compensation expense	\$4,048	\$4,579	\$7,572
Effect of stock-based compensation expense by line item:	19 C. 1	, t	· · ·
Research and development	\$3,074	\$3,503	\$5,779
General and administrative	974	1,076	1,793
Total stock-based compensation expense included in net income (loss)	\$4,048	\$4,579	\$7,572

Unrecognized stock-based compensation expense as of December 31, 2010 was as follows (in thousands):

	Unrecognized stock compensation	Weighted average
n terrer agen de la constante d En la constante de la constante	expense as of December 31, 2010	remaining period (in years)
Employee stock options	\$4,111 222	1.79 1.38
Total	 \$4,333	1.77

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 will receive a tax deduction. The Company does not record tax benefits related to ISOs unless and until a qualifying disposition occurs. 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 Income (Loss)**

Comprehensive income (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

### Notes to Consolidated Financial Statements (Continued)

### (2) Summary of Significant Accounting Policies (Continued)

unrealized gains and losses on marketable securities represent the only difference between the Company's net income (loss) and comprehensive income (loss).

### 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 Earnings (Loss) Per Common Share**

Basic net income (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 income (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.

For the years ended December 31, 2010, 2009 and 2008, common stock options calculated on a weighted average basis with exercise prices greater than the average market prices of the Company's common stock for these periods are not included in the computation of diluted earnings per share as their impact would have been anti-dilutive.

For the years ended December 31, 2010 and 2008, 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.

The following table sets forth the computation for basic and diluted net income (loss) per common share (in thousands, except per share information):

	Years H	Ended December 31,		
	2010	2009	2008	
Income (Numerator): Net income (loss) for basic and diluted calculations	\$(37,467)	\$79,088	\$(92,618)	
Shares (Denominator): Weighted-average shares for basic net income (loss) per share Effect of dilutive securities	40,365	33,888 231	33,736 —	
Weighted-average shares for diluted net income (loss) per share Basic net income (loss) per common share	40,365 \$ (0.93)	34,119 \$ 2.33	33,736 \$ (2.75)	
Diluted net income (loss) per common share Outstanding securities not included in the computation of diluted net income (loss) per common share as their inclusion would be	\$ <b>(0.93)</b>	\$ 2.32	\$ (2.75)	
anti-dilutive:   Common stock options   Unvested restricted stock	5,327 141	3,899 46	4,691 173	
	5,468	3,945	4,864	

### Notes to Consolidated Financial Statements (Continued)

## (2) Summary of Significant Accounting Policies (Continued)

## **Recent Accounting Pronouncements**

In April 2010, the Financial Accounting Standards Board, or FASB, issued Accounting Standard Update No. 2010-17, *Milestone Method of Revenue Recognition* ("ASU No. 2010-17"), which provides guidance on defining a milestone and determining when it may be appropriate to apply the milestone method of revenue recognition for research or development transactions. Prior to the issuance of ASU No. 2010-17, authoritative guidance on the use of the milestone method did not exist. ASU No. 2010-17 is effective on a prospective basis for milestones achieved in fiscal years, and interim periods within those years, beginning on or after June 15, 2010 with early adoption permitted. Alternatively, ASU No. 2010-17 can be adopted retrospectively for all prior periods. The Company's historical policy is such that, upon the achievement of milestones, revenue is recognized to the extent the accumulated service time, if any, has occurred. The remainder is deferred and recognized as revenue ratably over the remaining estimated performance period. The Company is currently evaluating how it will adopt ASU No. 2010-17 and whether it will have a material impact on its financial statements or results of operations.

In October 2009, the FASB issued Accounting Standard Update No. 2009-13, *Multiple-Element Revenue Arrangements* ("ASU No. 2009-13"), which updates the existing multiple-element revenue arrangements guidance currently included in Accounting Standards Codification No. 605-25 in two ways. The first change relates to the determination of when the individual deliverables included in a multiple-element arrangement may be treated as separate units of accounting. This is significant as it will likely result in the requirement to separate more deliverables within an arrangement, ultimately leading to less revenue deferral. The second change modifies the manner in which the transaction consideration is allocated across the separately identified deliverables. ASU No. 2009-13 also significantly expands the disclosures required for multiple-element revenue arrangements. ASU No. 2009-13 will be effective for the first annual reporting period beginning on or after June 15, 2010, and may be applied retrospectively for all periods presented or prospectively to arrangements entered into or materially modified after the adoption date. The Company does not expect ASU No. 2009-13 to have a material impact on its financial statements or results of operations.

# Notes to Consolidated Financial Statements (Continued)

# (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, 2010 and 2009 was as follows:

in the fil

en e	. v <sup>a</sup> .	December	31, 2010	the second second
	Cost	Unrealized gains	Unrealized losses	Fair value
	a sata	(in thou	usands)	and the state
Cash and cash equivalents: Cash and money market funds (Level 1)	\$25,228	\$	\$—	\$25,228
U.S. government-sponsored entities and corporate debt	. An look	ter tar tar		
securities due within 3 months of date of purchase (Level 2)	6,082		· · · · ·	6,082
Total cash and cash equivalents	31,310	<b>\$</b> —	<b>\$</b> —	\$31,310
Marketable securities:				and a start of the
U.S. government and government sponsored entities due within 1 year of date of purchase (Level 2)	19,666		(3)	19,663
Total cash, cash equivalents and marketable securities	\$50,976	\$ <u> </u>	<u>\$(3)</u>	<u>\$50,973</u>
and the second		1.1		
			r 31, 2009	
1. A set of the se	Cost	Unrealized gains	Unrealized losses	Fair value
		(in tho	usands)	0.34
Cash and cash equivalents: Cash and money market funds (Level 1)	\$36,367	\$	\$—	\$36,367
U.S. government-sponsored entities due within 3 months of date of purchase (Level 2)	7,788	· · · · ·	 . <u> </u>	7,788
Total cash and cash equivalents	<u>\$44,155</u>	<u>\$</u>	<u>\$</u>	<u>\$44,155</u>

# (4) Property and Equipment

Property and equipment consist of the following at December 31:

·	2010	2009	
	(in thousands)		
Laboratory equipment	\$ 12,387	\$ 12,337	
Leasehold improvements	4,528	4,495	
Computers and software	2,177	2,128	
Furniture and fixtures	1,050	1,046	
	20,142	20,006	
Less accumulated depreciation and amortization	(17,961)	(16,028)	
	\$ 2,181	\$ 3,978	

## Notes to Consolidated Financial Statements (Continued)

### (4) Property and Equipment (Continued)

Depreciation and amortization expenses of property and equipment, including equipment purchased under capital leases, were approximately \$1.9 million, \$2.5 million and \$2.7 million for the years ended December 31, 2010, 2009 and 2008, respectively.

The net book value and accumulated amortization of equipment under capital lease was \$0.4 million and \$0.9 million, respectively, at December 31, 2010, and \$2.1 million and \$8.9 million, respectively, at December 31, 2009.

#### (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.

## **Subscription Agreement**

In November 2010, the Company entered into a subscription agreement with a director and largest existing stockholder, pursuant to which the Company sold 1,440,923 shares of its common stock (the "Shares") at a purchase price of \$3.47 per Share, which was the closing price of the Company's stock on the day prior to the sale. The Shares were sold directly to this director without a placement agent, underwriter, broker or dealer. The proceeds to the Company were approximately \$5.0 million after deducting estimated offering expenses payable by the Company.

#### **Equity Line of Credit**

On October 4, 2010, 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 sell, in its sole discretion, and Azimuth is 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 is fewer, over the 18-month term of the agreement. Each draw down is limited in size, unless otherwise mutually agreed by the parties, to the lesser of (i) certain agreed-upon draw down amounts (the largest of which is \$4.25 million), based on the threshold price selected by the Company for the draw down, and (ii) 2.5% of the Company's market capitalization at the time of such draw down. Azimuth is not required to purchase shares of the Company's common stock if the threshold price is less than \$2.00 per share. The per share price of the shares sold in each draw down will be determined based on the daily volume weighted average price of the Company's common stock on each trading day during the draw down period, less a discount ranging from 4.875% to 6%. The Purchase Agreement also provides that, from time to time and in the Company's sole discretion, the Company may grant Azimuth the right to exercise one or more options to purchase additional shares of common stock during each draw down pricing period for the amount of shares based upon the maximum option dollar amount and the option threshold price specified by the Company. There were no transaction fees or warrants issued by the

## Notes to Consolidated Financial Statements (Continued)

# (5) Stockholders' Equity (Continued)

Company to Azimuth in connection with execution of the Purchase Agreement. Shares under the Facility, if issued, will be registered under the Company's registration statement on Form S-3 declared effective by the Securities and Exchange Commission on August 28, 2008. Upon each sale of common stock to Azimuth, the Company will pay to Reedland Capital Partners a placement fee equal to 1.0% of the aggregate dollar amount received by the Company from such sale. To date, no shares have been sold to Azimuth under the Facility. The Purchase Agreement may be terminated by either party at any time.

### **Public Offering**

In January 2010, the Company raised approximately \$28.8 million in gross proceeds from the sale of an aggregate 6,388,889 shares of its common stock in a public offering at \$4.50 per share, including 5,555,556 shares in the initial closing and 833,333 shares in a second closing for the full exercise of the over-allotment option granted to the underwriters. The net offering proceeds after deducting approximately \$2.1 million in expenses for underwriters' discounts, fees and commissions, legal, accounting, printing and listing and filing fees, and miscellaneous expenses were approximately \$26.7 million.

#### (6) Stock Plans

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. A total of 6,400,000 shares of common stock have been reserved for issuance under the 2006 Stock Plan. In January 2011, the number of shares of common stock reserved for issuance under the 2006 Stock Plan was increased from 5,100,000 to 6,400,000 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 ratified by the board of directors in December 2010. The administration of the 2006 Stock Plan is under the general supervision of 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 vest over one to four years.

As of December 31, 2010, under its 2001 Stock Plan, which was terminated in March 2006, the Company had options outstanding to purchase 1,941,278 shares of its common stock and had no shares available for future issuance.

As of December 31, 2010, under its 2006 Stock Plan, the Company had options outstanding to purchase 3,385,701 shares of its common stock, had outstanding 140,613 restricted shares of common stock and had available 1,341,670 shares available for future issuance.

#### Notes to Consolidated Financial Statements (Continued)

## (6) Stock Plans (Continued)

The following table summarizes stock option activity during the year ended December 31, 2010:

	Shares available for grant	Shares	Weighted average exercise price	Weighted average remaining contractual life (years)	Aggregate intrinsic value
Outstanding at January 1	2,301,133	4,900,598	\$8.95		
Options granted(1)	(1,596,561)	1,415,842	4.01		
Options exercised	· · · · ·	(132,745)	2.38		
Options cancelled(1)	637,098	(856,716)	8.04		
Additional shares reserved				·	
Outstanding at December 31	1,341,670	5,326,979	\$7.95	5.97	\$5,498,840
Exercisable at December 31		3,864,699	<b>\$9.13</b>	4.85	\$2,994,375

(1) Shares available for grant include stock options and awards of restricted stock.

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 \$6.12 on December 31, 2010. The weighted-average grant date fair values of options granted during the years ended December 31, 2010, 2009 and 2008 were \$3.27, \$1.98 and \$5.47, respectively.

The total intrinsic value of options exercised during the years ended December 31, 2010, 2009 and 2008 was approximately \$278,000, \$30,000 and \$4,000, respectively.

As of December 31, 2010, the total amount of unrecognized stock-based compensation expense was \$4.3 million, which will be recognized over a weighted average period of 1.77 years.

Included in the Company's stock options outstanding at December 31, 2010 were 157,555 options issued to non-employee consultants with a weighted average exercise price of \$8.84 of which all were vested. The compensation expense was recorded over the respective vesting periods and was subject to variable accounting treatment prior to vesting, whereby the Company remeasured the fair value of the options at the end of each reporting period. Changes in the fair value may result in an expense or a credit in each reporting period. Compensation expense related to these options was approximately \$0, \$17,000 and \$588,000, including the \$553,000 correction referred to in Note 2 in the years ended December 31, 2010, 2009 and 2008, respectively.

### 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 senior management and non-employee directors. Restricted stock awards are subject to forfeiture if employment or service terminates during the prescribed retention period. Restricted shares issued to non-employee directors and senior management vest over the service period. The remaining unrecognized compensation expense on restricted stock at December 31, 2010 was \$222,000. The weighted average period over which the balance is expected to be recognized is 1.38 years.

#### Notes to Consolidated Financial Statements (Continued)

## (6) Stock Plans (Continued)

The following table summarizes unvested restricted shares during the year ended December 31, 2010:

• .	en e	Shares	Weighted average grant date fair value
	Outstanding at January 1	48,107	\$5.14
	Granted	180,719	3.72
	Vested	(56,842)	
	Cancelled	(31,371)	5.48
	Outstanding at December 31	140,613	<u>\$3.84</u>
,			19 <sup>1</sup>

## (7) Other Accrued Liabilities

Other accrued liabilities consist of the following at December 31:

			·.·		• , · .	÷.,	: <sup>.</sup>	1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	2010	2009
									(in tho	usands)
Compens	ation and b	enefits		• • • •					\$2,903	\$2,792
Professio	nal fees				• • • • •				921	1,229
	••••									
an an an tao a		A seconda					÷	n an	\$4,194	\$4,504

#### (8) Collaborative License Agreement with Roche

In December 2008, as amended in February 2010 and February 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 is 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 consists 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 based upon research and development plans agreed to by the parties. These costs included committed research support over the initial two year research term that concluded on December 31, 2010. As of December 31, 2010, the Company has received approximately \$21.1 million in research and development support under the Roche Agreement. The Company does not expect to receive any additional research and development support under the Roche Agreement in 2011. Roche received worldwide rights to develop and commercialize certain products, referred to as Licensed Compounds, which were identified and studied prior to the end of the initial two year research term. For these Licensed Compounds, Roche is responsible for development and commercialization, while the Company retains certain co-development and co-promotion rights. In February 2011, the Roche

### Notes to Consolidated Financial Statements (Continued)

#### (8) Collaborative License Agreement with Roche (Continued)

Agreement was amended to extend the term of the research license to enable Roche to continue performing research on certain compounds until June 30, 2011. The amendment also provided for the return to the Company of certain Licensed Compounds. The Company retains all development and commercialization rights for its CRACM inhibitor compounds other than the specified Licensed Compounds licensed to Roche under the Roche Agreement.

The Company is also eligible to receive additional payments, for each of three licensed products, should specified development and commercialization milestones be successfully achieved. Development milestones across multiple indications of up to \$245 million could be earned for the first product, and up to half of this amount could be earned for each of the second and third products. Commercialization milestones of up to \$170 million could be earned for each of three products. The Company will receive tiered royalties on sales of all approved, marketed products. Roche may terminate the agreement on a licensed compound-by-compound basis upon providing advance written notice.

The \$16 million non-refundable upfront license payment is being recognized ratably using the time-based model over the estimated performance period through June 2012. In the years ended December 31, 2010, 2009 and 2008, the Company recognized \$4.6 million, \$4.6 million and \$0.1 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, 2010, 2009 and 2008, the Company recognized \$9.3 million, \$11.9 million and \$0, respectively, of cost sharing revenue under the Roche Agreement. As the initial research term concluded in December 2010, the Company does not expect to earn any cost sharing revenue under the Roche Agreement in 2011. Development milestones will be recognized as collaboration revenue using the time-based model over the same performance period. No development milestones have been achieved as of December 31, 2010.

# (9) Collaborative Development, Commercialization and License Agreement with GSK

In 2007, the Company and GSK entered into a global collaborative development, commercialization and license agreement (the GSK Agreement) for the joint development and commercialization of elesclomol. The GSK Agreement consisted of the following funding streams: an upfront license payment, product development milestones, operational milestones, reimbursements of certain development costs, sales milestones, profit sharing payments and product royalty payments. In 2009, following the suspension of the Company's global Phase 3 clinical trial of elesclomol plus paclitaxel in metastatic melanoma, called the SYMMETRY trial, GSK terminated the GSK Agreement effective September 10, 2009. In accordance with the termination provisions of the GSK Agreement, all rights to the elesclomol program were returned to the Company. The Company 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.

The \$80 million non-refundable upfront license payment, together with \$50 million in non-refundable operational milestones, the Company received from GSK were being recognized ratably using the time-based model over the estimated 15-year performance period. In the years ended December 31, 2009 and 2008, the Company recognized \$121.1 million and \$8.4 million, respectively, of license and milestone revenue under the GSK Agreement. Upon the effectiveness of the termination of

#### Notes to Consolidated Financial Statements (Continued)

## (9) Collaborative Development, Commercialization and License Agreement with GSK (Continued)

the GSK Agreement in the third quarter of 2009, the Company accelerated the recognition of approximately \$114.6 million of remaining deferred revenue from upfront payments and milestones received under the GSK Agreement as it had no further obligation for deliverables under the GSK Agreement.

Certain costs incurred by GSK, which related to the development of elesclomol in metastatic melanoma, were the Company's responsibility and had been recognized as a reduction of revenue under the GSK Agreement in the statement of operations. In the years ended December 31, 2009 and 2008, the Company recognized, as a reduction to revenue, \$4.1 million and \$5.9 million, respectively, of net cost sharing reimbursements to GSK under the GSK Agreement. The requirement to pay the cumulative GSK cost sharing reimbursements did not survive termination of the GSK Agreement and in the third quarter of 2009, upon the effectiveness of the termination of the GSK Agreement, the Company reversed approximately \$10 million of cost sharing reimbursement liabilities as collaboration revenue.

## (10) Restructuring

On March 12, 2009, the Company committed to a restructuring plan that consisted primarily of an immediate workforce reduction of approximately 90 positions, to a total of approximately 130 positions, to align its workforce to its revised operating plans following the suspension of its SYMMETRY clinical trial. In the first quarter of 2009, the Company recorded a restructuring charge of approximately \$1.2 million for severance and estimated benefits continuation costs and outplacement services. In addition, the Company paid approximately \$0.2 million in unused paid-time off that had been recognized as expense prior to the restructuring, including \$0.1 million in the year ended December 31, 2008 and \$0.1 million in the first quarter of 2009. The approximate \$1.4 million in restructuring related payments for severance, unused paid-time off, benefits and outplacement services was paid in 2009.

To conserve additional capital resources, the Company did not renew one of its office building leases that expired in August 2009 and consolidated its operations within its three other facilities. The Company did not incur an impairment charge in connection with the facility consolidation.

### Notes to Consolidated Financial Statements (Continued)

(1) 建立公司有限的合理公司

## (11) 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 ende	d December :	31,
	2010	2009	2008
	(in t	housands)	
Provision (benefit) at statutory rate	. \$(12,739) \$	26,890 \$(	(31,497)
State taxes, net of federal benefit		5,576	(5,453)
State tax rate change	. 196	2,129	. <u> </u>
State net operating loss expiration		1,292	1,508
Stock-based compensation	. 791	2,251	1,852
Tax credits	. (1,686)	(1,886)	(2,314)
Other	. (78)	96	459
(Decrease) increase in valuation allowance	. 11,663 (	36,348)	35,445
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:

	2010	2009
	(in thou	sands)
Deferred tax assets:		
Federal and state net operating loss carryforwards		\$ 95,351
Federal and state research and experimentation credits	15,250	13,737
Deferred revenue	2,652	4,507
Depreciation and amortization	2,769	2,713
Deferred compensation	4,641	4,164
Other	441	202
Deferred tax assets	132,338	120,674
Less valuation allowance	(132,338)	(120,674)
Net deferred tax assets	<u>\$                                    </u>	<u>\$                                    </u>

The total valuation allowance increased by approximately \$11.7 million in the year ended December 31, 2010, decreased by approximately \$36.3 million in the year ended December 31, 2009 and increased by approximately \$35.4 million in the year ended December 31, 2008.

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.

#### Notes to Consolidated Financial Statements (Continued)

### (11) Income Taxes (Continued)

In 2005, 2007, and 2010 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 limited. As of December 31, 2010, the Company has net operating loss carryforwards for U.S. federal tax purposes of approximately \$288.6 million, after excluding net operating loss carryforwards of approximately \$160.4 million, which will expire through 2014 unless utilized. 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 \$66.1 million of state net operating loss carryforwards expired in 2010.

At December 31, 2010, the Company had approximately \$12.0 million and \$4.9 million, respectively, in federal and state research and development credits which expire through 2030 and 2025, respectively.

The Company does not consider any of its tax positions to be uncertain and accordingly there are no tax reserves.

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 2007 through 2010. 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.

#### (12) Commitments and Contingencies

#### Leases

The Company leases its research and office facilities under non-cancelable operating leases with terms expiring in 2011. The Company is currently in negotiations to renew its expiring leases under its existing renewal options. Each of these leases contains renewal options ranging from one to five years. The Company also leases equipment under various other non-cancellable operating leases.

#### Term Loan with General Electric Capital Corporation

On September 30, 2010, the Company entered into a \$15 million loan and security agreement with GECC and one other lender, all of which was funded at the closing on September 30, 2010 (the GECC Term Loan). Interest on the borrowings under the GECC Term Loan accrues at an annual rate of 9.75%. The Company will make interest-only payments through June 2011, followed by 27 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 fees in the amount of \$150,000 and is obligated to pay an exit fee of \$450,000 at the time of the final payment of the outstanding principal. These amounts are being amortized and accreted, respectively, to interest

### Notes to Consolidated Financial Statements (Continued)

### (12) Commitments and Contingencies (Continued)

expense over the term of the GECC Term Loan. The Company paid approximately \$177,000 of legal fees and expenses in connection with the GECC Term Loan. These expenses have been deferred and, together with the \$150,000 origination fees, are included in other assets, and will be expensed over the term of the GECC Term Loan. In the year ended December 31, 2010, the Company recognized approximately \$67,000 in interest expense in connection with these origination, exit and transaction fees and expenses. In the year ended December 31, 2010, the Company recognized approximately \$453,000 in interest expense related to 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 burn covenants, as defined. The GECC Term Loan contains restrictive covenants, including the requirement for the Company 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. 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 was required to repay approximately \$787,000 of remaining principal outstanding under its existing equipment leases with GECC.

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

an <mark>an an a</mark>	$e_{1}e_{1}^{(1)}=e_{1}e_{1}e_{2}^{(1)}+e_{2}e_{2}^{(1)}e_{2}^{(1)}e_{2}^{(1)}$		Capital leases	Operating leases	GECC Term Loan
Years ending December 31,	•				
2011			\$ 208	\$1,717	\$ 4,711
2012			13	28	7,462
2013	· · · · · · · · · · · · ·		13	19	5,613
Total minimum payments			234	\$1,764	17,786
Less: amount representing interest	· · · · · · · · · · · · ·	••••	(7)		(2,786)
Present value of minimum payments			227		15,000
Less current portions of obligations					(3,333)
Long term obligation			\$ 26	,	\$11,667

Rent expense under operating leases was approximately \$2.0 million, \$2.6 million and \$2.5 million, for the years ended December 31, 2010, 2009 and 2008, respectively.

### Notes to Consolidated Financial Statements (Continued)

#### (12) Commitments and Contingencies (Continued)

License Agreements

#### **Beth Israel Deaconess Medical Center**

The Company acquired an exclusive license from Beth Israel Deaconess Medical Center (Beth Israel) relating primarily to ion channel technologies. Under the terms of the license, if certain milestones are met, the Company is required to make cash payments up to an aggregate of \$1.0 million. If commercialization is achieved, the Company will be required to pay royalties on the net sales of any product using the licensed technology. In the event the Company grants a sublicense of the licensed technology, the Company is obligated to compensate Beth Israel a percentage of all fees received from the sublicense. Through December 31, 2010, no milestone, royalty or sublicense payments had been earned by or paid to Beth Israel.

# **Consulting Agreements**

In October 2002, the Company entered into a consulting agreement with a Scientific Advisory Board, or SAB, member for scientific advisory services which was amended in October 2003. Under the amended consulting agreement, the term was four years from the effective date of the amendment, and in exchange for a one-time payment of \$400,000, the parties agreed to eliminate a one-time bonus payment to the SAB member based on the achievement of a certain performance milestone that was included in the original agreement. In addition to an annual consulting fee, the consultant was entitled to a bonus payment of a portion of any upfront or milestone payments received by the Company related to certain calcium channel technology during the four-year term of the amended agreement. In April 2007, the Company further amended this consulting agreement for a two-year term from the effective date of the amendment. In addition to the annual consulting fee, the consultant is entitled to potential bonus payments upon the Company entering into a partnership for certain calcium channel technology and upon the filing of an investigational new drug application (IND) with the FDA for a drug candidate developed under such a partnership. In connection with the Roche Agreement entered into in December 2008, the Company recorded a \$250,000 fee to this consultant in the year ended December 31, 2008. This corresponding payment was made in January 2009. In April 2009, the Company extended the consulting agreement until December 31, 2010.

#### 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 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 trials 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 has agreed to indemnify Roche and its affiliates under the Roche Agreement against losses, expenses, cost of defense, and any amounts Roche becomes legally

#### Notes to Consolidated Financial Statements (Continued)

## (12) Commitments and Contingencies (Continued)

obligated to pay because of any claim that arises out of the breach of any representation or warranty made by the Company under the Roche Agreement, except to the extent that such losses are due to the gross negligence or willful misconduct of Roche or the breach by Roche of any representation or warranty under the Roche Agreement. The Company also expects to agree to certain indemnification provisions in any future drug discovery and development collaboration agreements. 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 its 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 purchased 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. 

#### (13) 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, 2010, 2009 and 2008.

In November 2010, the Company entered into a subscription agreement with a director and largest existing stockholder (see Note 5).

#### (14) 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, 2010, 2009 and 2008 were approximately \$429,000, \$426,000 and \$514,000, respectively, subject to forfeitures.

# Notes to Consolidated Financial Statements (Continued)

# (15) Quarterly Financial Data (unaudited)

The following tables present a summary of quarterly results of operations for 2010 and 2009:

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		· · ·						1.1.1.1
		e se e la c	]	Three Mon	ths <b>E</b>	nded		·, ··
		rch 31, 2010		ne 30, 010	Sep	tember 30, 2010	Dec	ember 31, 2010
· "你们,你们们就是你们的你们。""你们还是我的人,你就能能不是你。" "你们我们,你们就是你们的你?""你们,你们就是我的人,你能能能不是你?"		(in tho	usands,	except sha	ires a	and per share	e data	)
Revenues:	• * .			· · ·			•	·
License and milestone revenue	\$	1,143	\$	1,143	\$	1,143	\$	1,143
Cost sharing reimbursements, net		2,880		2,217		2,240		1,916
Total collaboration revenues		4,023		3,360		3,383		3,059
Grant revenue				. —			;	978
Total revenues		4,023	:	3,360		3,383		4,037
Operating expenses:		Toops.	; ;	• N	1		·	a îtra
Research and development	. K	10,195	5 - J	9,688		11,023		9,347
General and administrative	1.2.1	3,086		2,716	· _ :	2,591		3,055
Total operating expenses		13,281		12,404		13,614		12,402
Loss from operations		(9,258)		(9,044)		(10,231)		(8,365)
Other expense, net		(50)		(30)	:	(31)		(458
Net loss	\$	(9,308)	\$	(9,074)	\$	(10,262)	\$ ·	(8,823)
Basic and diluted net loss per common share	\$	(0.24)	\$	(0.22)	\$	(0.25)	\$	(0.21
Basic and diluted weighted average number of		<u>.</u>		,		· ` ., · ·	• •	·
common shares outstanding	39,	451,592	40,3	342,671	4(	0,382,862	41	,263,628
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# Notes to Consolidated Financial Statements (Continued)

# (15) Quarterly Financial Data (unaudited) (Continued)

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	Three Months Ended							
· · ·	March 31, 2009	June 30, September 2009 2009		December 31, 2009				
	(in tho	usands, except sh	ares and per shar	e data)				
Collaboration revenues: License and milestone revenue Cost sharing reimbursements, net	\$ 4,073 437	\$ 3,314 1,336	\$ 117,171 13,234	\$     1,143 3,537				
Total collaboration revenues	4,510	4,650	130,405	4,680				
Operating expenses: Research and development General and administrative Restructuring (Note 11)	22,639 4,070 1,236	10,098 3,005 	9,084 3,149	9,234 2,426				
Total operating expenses	27,945	13,103	12,233	11,660				
Income (loss) from operations	(23,435) (64)	(8,453)	118,172 (53)	(6,980) (57)				
Net income (loss)	\$ (23,499)	\$ (8,495)	\$ 118,119	\$ (7,037)				
Net income (loss) per common share: Basic	\$ (0.69)		\$ 3.49	\$ (0.21)				
Diluted	<u>\$ (0.69</u> )	<u>\$ (0.25)</u>	\$ 3.48	\$ (0.21)				
Weighted-average common shares outstanding:BasicDiluted	33,872,016 33,872,016	33,877,075 33,877,075	33,882,760 33,904,842	33,918,887 33,918,887				