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CHELSEA  
THERAPEUTICS

*Annual Report* 10

## Fellow Stockholders,

Our unwavering commitment to the development of Northera™ (droxidopa) for the treatment of symptomatic neurogenic orthostatic hypotension (NOH) in 2010 culminated in the success of the largest trial ever undertaken in this indication, offering new hope for patients struggling with this condition and allowing us to move ahead in our plans to bring Northera to the US market.

### *Rising to the Challenge in 2010*

At the beginning of the year, our challenge was clear: incorporate the key discoveries from our first Phase III trial, Study 302, into our ongoing Phase III trial, Study 301, to provide for the strongest opportunity to clearly demonstrate the profound therapeutic benefit of Northera and ensure that our plans to bring Northera to market remained firmly on track.

Our team moved swiftly to integrate changes to Study 301, reach agreement with the FDA on the protocol for a new trial, Study 306, and to secure physician and patient participation in both studies.

These efforts clearly paid off in September when we announced the positive findings from Study 301 showing Northera treatment resulted in statistically significant improvements across the broad range of signs and symptoms of NOH. Together with the clinically meaningful benefits previously demonstrated in Study 302, we believe these results show the unprecedented symptomatic benefit of Northera and provided validation of its unparalleled safety and tolerability as a treatment option in this indication.

### *Revolutionizing the Treatment of NOH*

In addition to becoming the first drug to demonstrate symptomatic improvement of NOH in multiple studies, Northera continues to break new ground in our clinical research trials.

Recently reported data suggests that in addition to improving the classic signs and symptoms of NOH, including dizziness and difficulty standing or walking for short periods, Northera appears to dramatically reduce the number of falls experienced by patients with NOH associated with Parkinson's disease (PD).

Falling is among the most common, devastating and costly health risks faced by these patients. Injuries sustained in falls are a source of serious morbidity and mortality and are the leading cause for hospitalization and second most common reason for admission to institutional care.

Given the devastating impact of falls and the potential of Northera to reduce the number of falls resulting from NOH in PD, we are modifying our ongoing Phase III trial with the hope of validating these findings and ultimately expanding the future label of Northera to include both the improvement in symptoms of NOH and the reduction in falls associated with NOH associated with PD.

### *Advancing the Pipeline For Future Growth*

While the advancements in our NOH development program continued to garner the most attention in 2010, they were by no means our only achievements during the year.

Having progressed ahead of schedule in our Phase II trial of our novel, metabolically inert antifolate, CH-4051, in rheumatoid arthritis (RA), we are poised to report our first comparative data against methotrexate in RA patients later this year. There is a significant unmet medical need for safe and effective treatment options for RA patients who fail to achieve a good clinical outcome on methotrexate and we believe that the results of our Phase II trial will highlight the disease modifying potential of CH-4051 for patients who respond poorly to methotrexate.

Additionally, both through collaboration with leading clinicians and through our own development initiatives, we continued to advance the evaluation of droxidopa in several meaningful indications beyond NOH including: fibromyalgia, adult attention deficit disorder and chronic fatigue syndrome. Though more exploratory in nature, we remain excited by the potentially broad therapeutic benefits of norepinephrine replacement therapy with droxidopa and look forward to the insight these studies should afford us in this regard.

### *Looking Ahead*

Over the next year, our focus will be finalizing our Northera NDA for submission to the FDA, preparing for the anticipated commercial launch of Northera in the US, continuing to demonstrate the full therapeutic breadth of our pipeline and exploring potential partnership opportunities.

I would like to thank each of our shareholders, employees, physician partners and patients we hope to serve for their continued support of our efforts.



Dr. Simon Pedder, PhD  
President & Chief Executive Officer

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

FORM 10-K/A  
Amendment No. 1

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

FOR THE FISCAL YEAR ENDED DECEMBER 31, 2010, OR

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

FOR THE TRANSITION PERIOD FROM \_\_\_\_\_ TO \_\_\_\_\_

Commission file number 000-51462

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD.**

(Exact name of Registrant as specified in its charter)

Delaware  
(State or other jurisdiction of  
incorporation or organization)

20-3174202  
(I.R.S. Employer Identification No.)

3530 Toringdon Way, Suite 200, Charlotte, North Carolina 28277

(Address of principal executive offices, including zip code)

(704) 341-1516

(Registrant's telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Common Stock, \$0.0001 Par Value	Nasdaq Capital Market

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

None

Indicate by check mark if the Registrant is a well-known seasoned issuer (as defined in Rule 405 of the Securities Act).

Yes  No

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act.

Yes  No

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

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

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

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

Large accelerated filer

Accelerated filer

Non-accelerated filer

Smaller reporting company

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

The aggregate market value of the registrant's common stock held by non-affiliates of the Registrant, based on the closing price of the Registrant's common stock on June 30, 2010 (\$2.93 per share) was approximately \$88,800,000. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

At March 2, 2011, 61,846,919 shares of the Registrant's common stock, \$.0001 par value per share, were outstanding.

**Documents Incorporated By Reference**

Portions of the Registrant's definitive Proxy Statement to be filed for its 2011 Annual Meeting of Stockholders currently scheduled to be held May 18, 2011 are incorporated by reference into Part III of this report.



## EXPLANATORY NOTE

This Amendment No. 1 to the Annual Report on Form 10-K/A for Chelsea Therapeutics International, Ltd. amends our Annual Report on Form 10-K for the year ended December 31, 2010 initially filed with the Securities and Exchange Commission on March 2, 2011 (the “Original Filing”).

This Amendment No. 1 is being filed to amend Item 15—Exhibits and Financial Statement Schedules to include the Report of Independent Registered Public Accounting Firm dated March 10, 2008, of our previous independent registered public accounting firm, J.H. Cohn LLP, which was omitted from the Original Filing. This Amendment No. 1 also includes consents from Ernst & Young LLP (our current independent registered public accounting firm) as Exhibit 23.1 and J.H. Cohn LLP as Exhibit 23.2. Furthermore, we have updated (i) the index to the Financial Statements in Item 15(a)—Exhibits and Financial Statement Schedules—Financial Statements to include the report of J.H. Cohn LLP and (ii) the exhibit index in Item 15(b)—Exhibits and Financial Statement Schedules—Exhibits to include the consent of J.H. Cohn LLP.

This Amendment No. 1 includes currently dated certifications from the Company’s Chief Executive Officer and Chief Financial Officer, as required by Sections 302 and 906 of the Sarbanes-Oxley Act of 2002, attached as Exhibits 31.1, 31.2, 32.1 and 32.2 to this Amendment No. 1.

Except as set forth above, the Original Filing has not been amended, updated or otherwise modified. This Amendment No. 1 does not reflect events occurring after March 2, 2011, the date of the Original Filing, or modify or update those disclosures that may have been affected by subsequent events.

# ANNUAL REPORT ON FORM 10-K/A

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## PART I

**Except for the historical information contained herein, the matters set forth in this Report include forward-looking statements within the meaning of the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially. These risks and uncertainties are detailed throughout the report and will be further discussed from time to time in our periodic reports filed with the Securities and Exchange Commission. The forward-looking statements included in this Report speak only as of the date hereof.**

### ITEM 1. BUSINESS.

#### Overview

We are a development-stage pharmaceutical company that seeks to acquire, develop and commercialize innovative products for the treatment of a variety of human diseases. Our strategy is to develop technologies that address important unmet medical needs or offer improved, cost-effective alternatives to current methods of treatment.

We are currently developing a novel therapeutic agent for the treatment of symptomatic neurogenic orthostatic hypotension, or NOH, associated with primary autonomic failure and falls related to NOH in Parkinson’s Disease, or PD, as well as other potentially norepinephrine-related conditions and diseases, including intradialytic hypotension, or IDH, fibromyalgia, adult attention deficit hyperactivity disorder, or ADHD, chronic fatigue syndrome, or CFS, freezing of gait in PD and Down syndrome. In addition, we are developing a portfolio of metabolically inert antifolates for the treatment of rheumatoid arthritis and are exploring potential applications in multiple other autoimmune disorders, including psoriasis, Crohn’s disease, uveitis, ankylosing spondylitis, inflammatory bowel disease, cancer and other immunological disorders.

#### Product Pipeline Highlights

Droxidopa, our most advanced investigational product candidate, is an orally active synthetic precursor of norepinephrine. To be marketed under the brand name Northera™, droxidopa is being developed for the treatment of symptomatic NOH in primary autonomic failure, a group of diseases that includes PD, multiple systems atrophy, or MSA, and pure autonomic failure, or PAF. In 2007, the U.S. Food and Drug Administration, or FDA, granted orphan drug status to Northera for the treatment of symptomatic NOH and the European Medicines Agency, or EMA, granted orphan medicinal product designation for the treatment of orthostatic hypotension in patients with PAF and MSA.

In Japan, Northera has been approved since 1989 and is marketed by Dainippon Sumitomo Pharma Co., Ltd., or DSP, for the treatment of symptomatic orthostatic hypotension, freezing of gait in PD and IDH. We are currently seeking to register Northera in the United States for the treatment of symptomatic NOH and are conducting Phase III trials designed to support a supplemental new drug application, or sNDA, for the prevention of falls related to NOH in PD. We intend to submit an NDA and seek marketing approval in the United States for Northera for the treatment of symptomatic NOH in 2011.

In addition to our clinical and registration programs for Northera, we continue to explore additional therapeutic applications for droxidopa, both as a monotherapy and in combination with dopa decarboxylase inhibitors, such as carbidopa, in both Company-sponsored and investigator-led Phase II trials. Currently, such trials are ongoing in fibromyalgia, ADHD and CFS. We are also planning similar trials in freezing of gait in PD and Down syndrome.

We are also developing a portfolio of molecules for the treatment of various autoimmune/inflammatory diseases. The most advanced platform is a portfolio of metabolically inert antifolate molecules engineered to

have potent anti-inflammatory and anti-tumor activity to treat a range of immunological disorders, including two clinical stage product candidates: CH-1504 and CH-4051. Both are orally available molecules with anti-inflammatory, autoimmune and anti-tumor properties that potently inhibit several key enzymes required for cell proliferation. Preclinical and clinical data to date suggests superior safety and tolerability, as well as increased potency versus methotrexate, or MTX, currently the leading antifolate treatment and standard of care for a broad range of abnormal cell proliferation diseases. Diseases that may potentially be treated with these compounds include rheumatoid arthritis, psoriasis, Crohn's disease, ankylosing spondylitis, uveitis, psoriatic arthritis and several different kinds of cancer.

Complementing our antifolate program is a second platform consisting of a portfolio of dihydroorotate dehydrogenase, or DHODH, inhibiting compounds known as the I-3D portfolio. Although we are currently performing no work on this portfolio, preclinical animal data has shown potential applications in autoimmune diseases and transplantation.

We also remain active in evaluating potential in-licensing and acquisition candidates to identify and acquire additional drug candidates as available funding might allow.

To date, we have not received approval for the sale of any of our drug candidates in any market and, therefore, have not generated any revenues from our drug candidates.

## **Our Strategy**

Our mission is to create long-term stockholder value by acquiring, developing and commercializing innovative products for the treatment of a variety of human diseases that address important unmet medical needs or offer improved, cost-effective alternatives to current methods of treatment. Since inception in 2002, we have focused primarily on organizing and staffing our company, negotiating in-licensing agreements with our partners, acquiring, developing and securing our proprietary technology, participating in regulatory discussions with the FDA, the EMA and other regulatory agencies, undertaking preclinical and clinical trials of our product candidates and raising capital. We are a development stage company and have generated no revenues since inception. We do not anticipate generating any product revenue until approvals are successfully obtained from the FDA or equivalent foreign regulatory bodies to begin selling pharmaceutical candidates.

We expect the progress of our development programs to be a primary factor affecting our expenses, losses and cash position in the future. During 2010 and in 2011, we have completed, are continuing to conduct our plan to conduct clinical trials as follows:

- Phase III clinical programs for Northera in symptomatic NOH for which patient recruiting was completed in 2010;
- a Phase III hypothesis-generating clinical program for Northera in the prevention of falls related to NOH in PD that completed enrollment in 2011 with 51 patients;
- an ongoing Phase III hypothesis-confirming clinical program for Northera in the prevention of falls related to NOH in PD, requiring a total of approximately 162 patients;
- an ongoing Phase II program for droxidopa, alone and in combination with carbidopa, in fibromyalgia, requiring a total of approximately 120 patients; and
- an ongoing Phase II program for CH-4051 in rheumatoid arthritis, requiring a total of approximately 250 patients.

We also continue to discuss our antifolate program with large pharmaceutical companies to gauge their interest in licensing this library of compounds. We believe a partner may be able to manage Phase III trials and global commercialization more effectively and with less risk than we could and, accordingly, our current strategy is to pursue such a partnership. Similarly, as we are currently not planning to establish commercial operations outside of the United States, we continue to discuss potential licensing arrangements for droxidopa in Europe and other markets outside the United States. In the course of these discussions, the program has generated interest

among potential partners and we continue to evaluate the licensing potential for droxidopa in North America. Any such partnership would aim to provide significant value to us and our stockholders, while maximizing the opportunities for droxidopa in global markets. We also continue to pursue and evaluate potential out-licensing arrangements for our I-3D portfolio of DHODH inhibiting compounds.

We have retained a management team with leading core competencies and expertise in numerous fields, including manufacturing, drug development, including preclinical and clinical, regulatory, sales, marketing, finance and business development. Our management and advisors are comprised of experienced pharmaceutical and biotechnology industry veterans and respected experts. We are led by our Chief Executive Officer, Dr. Simon Pedder, formerly Vice President, Pharmaceutical Business, Oncology at Hoffmann-La Roche Inc., who has over 20 years of senior pharmaceutical management experience, including drug development and business experience. During his time at Roche, Dr. Pedder was responsible for a number of global development programs, successful registrations and product launches.

### **Plan of Operation**

Our plan of operation is to continue implementing our business strategy, especially the clinical development of our current drug candidates including droxidopa and our portfolio of antifolates. As we have in the past, we plan to continue exploring the feasibility of other licensed or newly developed compounds and to expand our drug candidate portfolio by acquiring additional drug technologies for development as our resources permit. We expect our principal expenditures during the next 18 months to include:

- operating expenses, including general and administrative and business development expenses;
- marketing, sales and other pre-launch commercialization expenses for Northera; and
- product development expenses, including the costs incurred with respect to our clinical trials for droxidopa and our antifolates.

As part of meeting our operating needs and as resources permit, we may hire additional scientific, marketing, sales, operations and administrative staff. In addition, we intend to continue using clinical research organizations and third parties to perform our clinical studies and manufacturing.

### **Corporate History**

Our operating company was incorporated in Delaware in April 2002 under the name Aspen Therapeutics, Inc., and changed its name to Chelsea Therapeutics, Inc. in July 2004. On February 11, 2005, Chelsea Therapeutics, Inc. completed a merger with Ivory Capital Corporation, a publicly traded Colorado corporation formed in May 1988. At the time of the transaction, Ivory Capital had only nominal assets and no operating activities. In connection with this merger transaction, a wholly owned subsidiary of Ivory Capital Corporation merged with and into Chelsea Therapeutics, Inc., with Chelsea Therapeutics, Inc. remaining as the surviving corporation and a wholly owned subsidiary of Ivory Capital Corporation. In connection with the merger, the former stockholders of Chelsea Therapeutics, Inc. received 96.75% percent of our outstanding equity on a fully diluted basis. Pursuant to the terms of the merger, the sole officer and director of Ivory Capital Corporation prior to the merger was replaced with the officers and directors of Chelsea Therapeutics, Inc.

On June 17, 2005, Ivory Capital Corporation formed a wholly owned subsidiary in Delaware named Chelsea Therapeutics International, Ltd. for the purposes of reincorporating in Delaware. On July 28, 2005, Ivory Capital Corporation merged with Chelsea Therapeutics International, Ltd., with Chelsea Therapeutics International, Ltd. as the surviving corporation. As a result, Chelsea Therapeutics International, Ltd. is the public reporting company and is the 100% owner of Chelsea Therapeutics, Inc., its operating subsidiary.

Except where the context provides otherwise, references to “we,” “us,” “our” and similar terms mean Chelsea Therapeutics International, Ltd., Ivory Capital Corporation and Chelsea Therapeutics, Inc. When we

refer to business and financial information relating to periods prior to December 31, 2004, we are referring to the business and financial information of Chelsea Therapeutics, Inc. unless the context requires otherwise. When we refer to business and financial information for periods between January 1, 2005 and July 28, 2005, we are referring to the business and financial information of Ivory Capital Corporation.

## **Products Under Development**

### ***DROXIDOPA***

#### **Product Overview**

Droxidopa, a synthetic amino acid, is converted by the body into norepinephrine and, as a prodrug of norepinephrine, provides replacement therapy for norepinephrine deficiency. Norepinephrine is both a hormone and a neurotransmitter. As a hormone, secreted by the adrenal gland, it works alongside epinephrine/adrenaline to give the body sudden energy in times of stress, known as the “fight or flight” response. As a neurotransmitter, it passes nerve impulses from one neuron to the next. While norepinephrine, as a catecholamine does not penetrate the blood-brain barrier, droxidopa, as a neutral amino acid, is able to do so thus providing both a peripheral and central effect on circulating norepinephrine levels. By producing and replenishing depleted norepinephrine via endogenous enzymatic pathways, droxidopa is believed to allow for the re-uptake of norepinephrine into peripheral and central nervous system neurons.

Droxidopa is currently approved and marketed by Dainippon Sumitomo Pharma Co., Ltd., or DSP, in Japan for the treatment of symptomatic orthostatic hypotension, freezing of gait in PD and IDH. Droxidopa received initial Japanese marketing approval in 1989 and has historically generated annual revenues of approximately \$50 million in Japan. In addition to the indications studied by DSP and subsequently approved in Japan, diseases that may potentially be treated with droxidopa include fibromyalgia, CFS, ADHD, and other indications in which norepinephrine deficiencies are believed to play a role.

#### **Clinical Development**

We are currently focusing on the clinical development of droxidopa in symptomatic NOH, the prevention of falls related to NOH in PD, the treatment of fibromyalgia and IDH. In order to maximize the potential therapeutic applications of droxidopa while conserving capital, we currently support two investigator-sponsored studies of droxidopa in ADHD and CFS and plan to continue exploring opportunities to support additional, investigator-sponsored studies of droxidopa in indications for which we believe a strong clinical rationale exists.

#### *Neurogenic Orthostatic Hypotension*

Given the extensive body of clinical data generated by DSP and exclusivity available to us under terms of our licensing agreement, we plan to seek initial marketing approval of droxidopa, under the brand name Northera™, in the United States and European Union for the treatment of symptomatic NOH, an indication for which the drug has been approved in Japan since 1989.

Orthostatic hypotension is a sudden decrease in blood pressure when a person assumes a standing position and is characterized by lightheadedness, dizziness, blurred vision and syncope. There are multiple known causes for orthostatic hypotension including those that are considered cardiovascular, endocrine and neurological (or neurogenic) in nature. Orthostatic hypotension that is neurogenic in nature results from a deficient release and/or synthesis of norepinephrine, a neurotransmitter used by autonomic nerves to send signals to the blood vessels and the heart. This condition is commonly associated with PD, pure autonomic failure, or PAF, and multiple systems atrophy, or MSA, and has a significant impact on sufferers’ quality of life, with some patients unable to stand unaided for more than a few minutes a day.

In January 2007, the FDA granted orphan drug status for Northera for the treatment of symptomatic NOH in patients with primary autonomic failure, dopamine-β-hydroxylase deficiency and non-diabetic autonomic

neuropathy. In the United States, orphan drug status provides seven years of marketing exclusivity and may impact FDA requirements for clinical trials, potentially reducing the time and expense required for such trials. In August 2007, the EMA granted two orphan medicinal product designations for Northera for the treatment of orthostatic hypotension in patients with PAF and MSA. Although we can expect 10 years of data exclusivity for droxidopa upon approval in Europe as a new chemical entity, orphan drug status could impact requirements for clinical trials in Europe, thereby increasing the time and costs associated with our development of droxidopa for this market.

The FDA has also granted Fast Track designation to Northera for symptomatic NOH. Fast Track designation is designed to facilitate the review of products that address serious or potentially life-threatening conditions for which there is an unmet medical need. In addition, drugs that have Fast Track designation are more likely to be considered appropriate for Priority Review. A Priority Review generally reduces the time it takes the FDA to review an NDA.

We have previously completed two Phase III trials, Studies 301 and 302, of Northera for the treatment of symptomatic NOH in patients with primary autonomic failure. The improvements in the symptoms of NOH, as measured by the orthostatic hypotension questionnaire composite score, or OHQ composite, associated with Northera treatment in our pivotal efficacy Study 301 are highly significant ( $p < 0.003$ ) and showed similar improvements ( $p < 0.05$ ) in a post-hoc analysis of Study 302 data. On that basis, we proposed filing our NDA in symptomatic NOH. During our pre-NDA meeting in December of 2010, the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from our two completed Phase III studies of Northera in NOH, Study 301 and Study 302, and their associated safety Studies 303, 304 and 305, without the need for additional efficacy studies. During the meeting, the FDA did request and we agreed to supply top-line results from a QTc study at the time of the 90-day safety update. A QT interval is a measure of the time between the start of the Q wave and the end of the T wave in the heart's electrical cycle. In general, a prolonged QT interval is a biomarker for ventricular tachyarrhythmias and can be a risk factor for sudden death. In addition, the FDA also requested that we conduct a post-marketing study to evaluate the clinical pharmacology of Northera in renally-impaired patients.

Study 301 and Study 302 were designed to compare Northera to placebo at multiple sites in North America, Europe and Australia. Both Phase III trials were intended to assess the safety and efficacy of up to 600 mg t.i.d. of Northera in patients suffering from symptomatic NOH associated with primary autonomic failure and both were designed to evaluate functional and symptomatic improvements through multiple endpoints including OHQ scores.

In September 2010, we announced that a preliminary analysis of Study 301 showed the study had met its primary endpoint. Treatment with Northera provided clinically-meaningful and statistically-significant improvement ( $p = 0.003$ ) in symptoms associated with NOH. Study results also showed that Northera was both safe and very well tolerated. The 167 patients randomized into this double-blind, placebo-controlled study were evaluated for symptomatic and functional improvements using the OHQ composite, which is specifically designed to rate the severity of symptoms resulting from low-blood pressure and the degree to which those symptoms interfere with a patient's ability to perform activities of daily living. In addition to the symptomatic and functional benefits registered on the OHQ composite, the study validated Northera's unique mechanism of action and confirmed the preferential effect of Northera on standing systolic blood pressure, or SBP, versus supine SBP, demonstrating a statistically significant improvement in standing SBP ( $p < 0.001$ ) relative to placebo. The study was conducted under a Special Protocol Assessment, or SPA, granted by the FDA in February 2008, providing an agreement that the study design, including trial size, clinical endpoints and/or data analyses is acceptable to support regulatory approval.

The primary efficacy endpoint for Study 302 was defined as the relative symptomatic change, as measured by the mean score of Item 1 (dizziness or lightheadedness) of the Orthostatic Hypotension Symptom Assessment, or OHSA, 14 days following randomization either to continued therapy with droxidopa or to placebo. In

September 2009, we announced preliminary data from Study 302. While strong symptomatic benefit was demonstrated during the open-label dose titration and run-in phase of the trial, results of the trial did not demonstrate a statistically significant improvement relative to placebo, as measured by the study's primary efficacy endpoint. While the study did not meet its primary endpoint, additional analysis confirmed statistically significant symptomatic benefit across multiple, clinically relevant assessment criteria that reflect symptomatic improvements and corroborate other supportive symptom data, including a significant improvement in the OHQ composite ( $p < 0.05$ ) over placebo. Data from the trial also supported the safety and tolerability of Northera.

Anecdotal evidence in the adverse events reported in Study 302 suggested that Northera treatment was associated with fewer falls. Accordingly, we decided to prospectively assess this benefit as a secondary efficacy parameter in Study 306, a Phase III trial of Northera in PD patients with NOH initiated in 2010, upon the recommendation of the FDA and prior to the completion of Study 301. Study 306 was originally intended to support our registration of Northera for the treatment of NOH using the primary endpoint of the relative mean change in OHQ composite between treatment and placebo arms. In February 2011, we announced our plans to modify Study 306 following a futility determination at the planned interim analysis of the study's primary endpoint and an unblinded review of multiple, secondary outcome measures showing a 60% reduction in falls and supportive signs of therapeutic activity associated with Northera in the first 51 patients to complete Study 306. Given the highly significant outcome of Study 301, the FDA agreement that sufficient data exists to support an NDA filing without the results of Study 306 and given the outcome of the interim analysis, we now intend to modify Study 306 and use the data from this trial to form the basis for a future, supplemental claim of a reduction in falls associated with NOH in PD.

Having already enrolled 113 patients as of February 2011, we now plan to modify and separate Study 306 such that the first 51 patients evaluated in the unblinded interim analysis will be considered Part A (Study 306a) and constitute a hypothesis-generating study, and the remaining patients enrolled or to be enrolled in the study will become Part B (Study 306b) and serve as a distinct, hypothesis-confirming study. Based on the analysis of data from Study 306a, we currently plan to repower the study to demonstrate a 40% reduction in falls associated with NOH in PD and expect to add approximately 100 additional patients to the 62 blinded patients already enrolled in Study 306b. Based on these preliminary estimates, we anticipate data from Study 306b will likely be available by the second quarter of 2012. Collectively, we believe the results from Studies 306a and 306b should serve as the basis for a sNDA intended to expand the future labeling of Northera in the United States to include the prevention of falls in NOH associated with PD.

In addition to the efficacy trials included in our registration program, we have completed, are continuing to conduct, or plan to conduct multiple safety and extension studies designed to provide supportive safety data for our NDA in NOH. These studies include:

- Study 303: a renewable three-month, open-label extension to Study 302 which included a randomized withdrawal efficacy assessment after the initial three months and for which results were announced in May 2010;
- Study 304: a renewable three-month, open-label extension to Study 301 and Study 306 that remains ongoing for patients in the United States;
- Study 305: a 24-hour blood pressure monitoring study in a subgroup of 18 patients from Study 301 for which results were announced in March 2010; and
- Study QTC-102: a Phase I QTc prolongation study currently scheduled to begin in March 2011.

Results from our registration program, in combination with data secured from DSP, are expected to support an application for marketing approval, under the brand name Northera™ in the United States in 2011 with an anticipated market launch no earlier than the second quarter of 2012. Since an initial discussion in 2006, we have not conducted further discussions of the specifics of our clinical program with the EMA and we do not know if our current program will be acceptable for marketing approval in the European Union or if we may be required to conduct additional efficacy trials.

### *Intradialytic Hypotension*

IDH is another indication for which DSP conducted extensive clinical evaluation. Pivotal clinical studies conducted by DSP have demonstrated the efficacy of droxidopa in the prevention of vertigo, dizziness and weakness associated with hypotension in hemodialysis patients. Subsequently, in 2000, after showing benefit in clinical trials, DSP received expanded marketing approval in Japan for this indication.

Intradialytic hypotension is the most common adverse event during routine hemodialysis. IDH is often defined as a decrease in systolic blood pressure by  $\geq 20$  mm Hg or a decrease in mean arterial pressure by 10 mm Hg. IDH has been reported in 15-25% of all hemodialysis patients, with elderly patients reporting an even higher incidence. Many adverse hemodialysis events, including headaches, lightheadedness, nausea, cramps, and seizures, are associated with IDH. These complications can routinely interrupt dialysis sessions, resulting in insufficient uremia toxin removal and necessitating repetition of the procedure. Interruptions due to IDH increase the costs of both the dialysis treatment sessions and the long-term care of less healthy hemodialysis patients.

In March 2009, we reported results from a double-blind, placebo controlled trial comparing 400mg and 600mg of droxidopa to placebo. Following a two-week run-in period to establish a baseline for all measurements, patients in this three-arm study received a single oral dose of droxidopa or placebo one hour prior to each dialysis treatment over a four-week period. In order to determine useful clinical endpoints for a Phase III program, the trial evaluated the efficacy of droxidopa using multiple clinically relevant measures, including: the change from baseline in average mean arterial blood pressure during dialysis; the change from baseline in average mean nadir (lowest) blood pressure during dialysis; the number of treatment interventions, including early termination, required during dialysis sessions; and the change from baseline in mean postdialytic blood pressure during the final two weeks of the study period. The study recruited 85 patients at 15 sites in the United States. Droxidopa demonstrated a dose dependent, statistically significant benefit across multiple, clinically relevant assessment criteria for IDH. While the study did not achieve an improvement in mean arterial blood pressure during dialysis, the prospective primary endpoint for the study, droxidopa demonstrated a significant benefit in limiting the severity of the drop (nadir) in blood pressure during treatment. The data also showed that droxidopa was well tolerated by patients with the most common treatment-related side effect reported being headache (3%). Results from this study might be used to determine clinical endpoints for a potential future Phase III program that might allow us to file for the first marketing approval of a therapeutic agent for IDH in the United States.

### *Fibromyalgia*

Fibromyalgia is a polysymptomatic syndrome characterized by chronic, widespread musculoskeletal pain, multiple tender points, abnormal pain sensitivity, and is often accompanied by severe fatigue, insomnia and mood symptoms. According to the American College of Rheumatology, fibromyalgia is the second most commonly diagnosed condition in rheumatology clinics in the United States after osteoarthritis and is estimated to affect over six million Americans. While the precise etiology of fibromyalgia remains unknown, current research includes the role of norepinephrine reuptake and availability in the central nervous system. Norepinephrine, a widely used neurotransmitter in the central and peripheral nervous systems, has long been linked to both chronic pain and depression. While norepinephrine, as a catecholamine, does not penetrate the blood-brain barrier, droxidopa, as a neutral amino acid, is able to do so thus providing both a peripheral and central effect on circulating norepinephrine levels. In prior studies conducted by DSP, droxidopa has shown statistically significant dose-dependent analgesia in chronic pain.

In January 2009, we initiated a Phase II trial of droxidopa, both alone and in combination with carbidopa, for the treatment of fibromyalgia. In July 2010, we announced the completion and favorable outcome of an independent Data Monitoring Committee (DMC) review of the safety and efficacy data from approximately half the target enrollment. The purpose of this scheduled DMC meeting was to review the efficacy of each dose group and determine if the efficacy data supported dropping underperforming arms in order to increase the power in those arms most likely to demonstrate a clinically relevant therapeutic benefit. Following their assessment of each of the 12 arms using the study's primary endpoint, a reduction in pain as measured by the Short Form

McGill Pain Questionnaire, the DMC recommended that 7 of the 12 arms of the trial be continued to completion. This recommendation was based solely on their efficacy analysis, as there were no observed safety concerns associated with any arm of the study. As a result of this recommendation, the study will now focus primarily on multiple doses of droxidopa in combination with 50mg carbidopa. The Phase II trial, being conducted in the U.K., is a multi-center, randomized, double-blind, placebo-controlled, dose response, factorial parallel group study evaluating 120 patients equally randomized to receive droxidopa monotherapy, carbidopa monotherapy, droxidopa/carbidopa combination therapy or placebo over a 9-week treatment period. Secondary outcomes of the study include Fibromyalgia Index Questionnaire (FIQ), Patient Global Impression of Change (PGI-C), Multidimensional Fatigue Inventory (MFI), and Hamilton Anxiety Depression survey (HAMA). We currently do not anticipate completing this trial or reporting clinical results in this indication until 2011 at the earliest.

### **Additional Potential Indications for Droxidopa**

In addition to the indications for which we have established active clinical programs, we believe there are a significant number of other therapeutic indications in which norepinephrine function plays a key role and for which droxidopa may provide clinical benefit. To facilitate research in additional indications and maximize the long-term development potential, we have initiated an extra-mural development program that enables independent investigators to conduct clinical trials in their respective fields of expertise. Specifically, we have been exploring Phase II clinical studies, under investigator-sponsored investigational new drug applications, or INDs, intended to evaluate the safety and efficacy of droxidopa in ADHD, CFS, freezing of gait in PD and Down syndrome. For studies conducted under investigator-sponsored INDs, we have limited control over the timing for initiating or completing these studies and, therefore, cannot predict with any certainty when data from these programs will be available.

In February 2010, we announced that a new investigator-led Phase II clinical study of droxidopa, alone and in combination with carbidopa, in ADHD had been initiated by the Narrows Institute for Biomedical Research in New York. Based on current enrollment and feedback from the investigator, we currently expect data from this study to be available in the second quarter of 2012. In August 2010, we also announced that an investigator-led, open label Phase II study of droxidopa for the treatment of chronic fatigue syndrome, or CFS, had been initiated at the Hunter-Hopkins Center in Charlotte, North Carolina.

We plan to continue working with key opinion leaders to identify and evaluate additional potential indications for droxidopa and may provide droxidopa for future studies when deemed appropriate and as funding and availability of drug substance permits.

### **Droxidopa Competition**

#### *Neurogenic Orthostatic Hypotension*

#### **Midodrine** (ProAmatine®)

Midodrine is currently the only FDA-approved therapeutic for the treatment of orthostatic hypotension. Midodrine's product label contains a black box warning for the side effect of supine hypertension, along with the statement that midodrine has not shown benefit to patients' Activities of Daily Living, or symptomatic/functional benefit. In August 2010, the FDA indicated publicly that unless two studies are successfully completed within a specified timeframe to confirm the symptomatic benefit of midodrine, the agency will consider removing midodrine from the market. In January 2011, the FDA announced the opening of a public docket (FDA-2010-N-0637) to provide a forum to facilitate communication regarding the conduct of clinical trials needed to support continued marketing authorization for midodrine. As the only approved compound for orthostatic hypotension in the U.S, midodrine's removal could facilitate higher sales and/or more rapid acceptance of droxidopa in this indication. However, the FDA has never removed a drug under similar circumstances and we can provide no assurance that they will do so in the case of midodrine.

Other than the increase in blood pressure caused by vasoconstriction, additional midodrine side effects include paresthesia (tingling), piloerection (goosebumps), dysuria (painful urination), and pruritus (itching). Annual sales (branded and generic) in the United States total approximately \$38 million, based on 2009 data. In addition to Shire's manufacturing of the ProAmatine brand, Mylan Pharmaceuticals, Eon Labs and Impax Laboratories are generic manufacturers of the compound.

### **Fludrocortisone (Florinef®)**

Fludrocortisone is also widely used in the treatment of orthostatic hypotension although this specific indication has not been approved by the FDA. Fludrocortisone is a synthetic adrenocortical steroid possessing very potent mineralocorticoid properties and high glucocorticoid activity. Fludrocortisone, in small oral doses (0.1mg.) produces marked sodium retention and increased urinary potassium excretion leading to enhanced plasma volume and a rise in blood pressure. Side effects include hypertension, water and sodium retention and potassium, or K+, loss. Fludrocortisone is not FDA-approved for NOH.

### *Intradialytic Hypotension*

There is currently no FDA-approved drug for treatment or prevention of intradialytic hypotension. Common methods for treating IDH include the manual adjustment of ultrafiltration rate, a cumbersome procedure in daily practice. Some dialysis patients are known to take midodrine prophylactically, either before or during dialysis, to prevent intradialytic hypotension. However, midodrine is known to be eliminated through the kidneys and is removed by dialysis, thereby limiting its widespread use in this indication.

### *Fibromyalgia*

While doctors have used antidepressants and pain drugs for years, in June 2007, the FDA granted its first approval for the treatment of fibromyalgia to Pfizer's Lyrica®, which was already used to treat epilepsy and neuropathic pain. Worldwide sales of Lyrica® in 2009 totaled \$2.8 billion. Eli Lilly received approval in 2008 to market Cymbalta®, a selective serotonin and norepinephrine reuptake inhibitor, to treat fibromyalgia and generated worldwide sales in all indications of \$3.1 billion in 2009. Cypress Biosciences, with their partner Forest Laboratories, received FDA approval in early 2009 for Savella® for the treatment of fibromyalgia. Savella® is a norepinephrine serotonin reuptake inhibitor that increases the level of norepinephrine more than it does serotonin.

### **Droxidopa Marketing**

We currently estimate that nearly 400,000 patients suffer from chronic, symptomatic NOH in the United States and the European Union combined. This condition is commonly associated with PD, PAF and MSA, the latter encompassing disorders previously known as striatonigral degeneration, olivoponto-cerebellar atrophy and the Shy-Drager syndrome. In addition to the broader symptoms and impact on activities of daily living, NOH significantly increases the risk of falls in patients with PD and is believed to be responsible for significant healthcare costs due to the high incidence of falls-related injuries in this patient population, particularly in elderly patients. According to the Centers for Disease Control and Prevention, the cost of medical care for falls-related injuries was estimated to be approximately \$20 billion in 2000 and is estimated to grow to \$55 billion by 2020. The National Center for Injury Prevention and Control estimates this cost to be \$240 billion with over 500,000 hospitalizations in 2040. Preliminary data from our studies suggests that the use of Northera by patients with NOH associated with PD results in a meaningful reduction in falls in these patients. Reducing serious falls by 30% in this population, by our estimate, could result in a potential annual savings of approximately \$5 billion in falls-related costs, including the costs of extended care in skilled nursing facilities.

We do not currently have a commercial sales and marketing organization in any territory and do not plan to establish the necessary infrastructure to support future sales outside of the United States. As a result, we would

expect to partner with or license Northera to companies with established infrastructure in the European Union and other markets. With regard to the United States, we believe that the market for Northera in NOH, our most immediate commercial opportunity, could be addressed through the establishment of a marketing and sales organization on a stand-alone basis. During 2010, we conducted studies to further evaluate the marketing potential for Northera in the United States, the United Kingdom, Germany, France, Spain and Italy. The favorable results of these studies were suggestive of a potential and possibly significant market opportunity. Given this commercial opportunity and the nature of marketing a drug under orphan drug protection, there may exist opportunities for us to more effectively pursue co-marketing, co-promotion or other alliances within the United States.

It is possible that we might directly commercialize or co-promote droxidopa in IDH and other smaller potential therapeutic indications. Given the size of the fibromyalgia market, the vast sales forces required to compete in this market, and the necessary infrastructure required, our marketing strategy in this indication is likely to include contracting with or licensing to third parties, particularly for territories outside the United States. Out-licensing arrangements might be negotiated and entered into prior to droxidopa receiving marketing approval in one or more of the indications currently under clinical development

## ***METABOLICALLY INERT ANTIFOLATES***

### **Product Overview**

Our portfolio of novel antifolate compounds was originally developed by Dr. M. Gopal Nair and licensed to us in 2004. A library of orally available and metabolically inert antifolate compounds with potent autoimmune, anti-inflammatory and anti-tumor properties, these compounds are engineered to treat a broad range of immunological disorders with fewer harmful and unpleasant side effects than those typically associated with classical antifolates such as methotrexate, or MTX, currently the leading antifolate treatment and standard of care for a broad range of abnormal cell proliferation diseases.

Drug candidates from this portfolio, including both clinical candidates CH-1504 and CH-4051, inhibit dihydrofolate reductase, an enzyme required for cell proliferation, but, due to the lack of metabolism, are devoid of the metabolites believed to play a significant role in the liver and kidney toxicities associated with long-term use of MTX and show a clinically relevant decrease in toxicity compared to MTX.

We believe these unique antifolates might have clinical advantages over MTX as they might have less toxicity and increased tolerability while maintaining equal or potentially greater efficacy. Potential advantages over existing therapies, supported by our preclinical and clinical work to date, include:

- higher response rate, including efficacy in patients that have failed MTX therapy;
- faster onset of action;
- better tolerability; and
- superior toxicity profile.

Diseases that may potentially be treated with metabolically inert antifolates include rheumatoid arthritis, psoriasis, Crohn's disease, uveitis, ankylosing spondylitis, inflammatory bowel disease, cancer and other immunological disorders.

### **Clinical Development**

Our portfolio of drug candidates includes multiple molecules for the treatment of various autoimmune/inflammatory diseases. The most advanced platform is a portfolio of metabolically-inert antifolate molecules engineered to have potent anti-inflammatory and anti-tumor activity to treat a range of immunological disorders, including two clinical stage product candidates designated as CH-1504 and CH-4051. CH-1504 has completed

Phase II trials in rheumatoid arthritis. While we do not intend to conduct additional trials or make further investments in the development of CH-1504, clinical work related to this compound might provide meaningful informative data supporting the development of additional compounds in this portfolio. Based on preclinical and clinical findings to date, we intend to focus our clinical resources on the continued development of CH-4051, the second clinical stage compound in this portfolio and the more potent L-enantiomer of CH-1504. CH-4051 is currently being developed with a lead indication of rheumatoid arthritis, having completed a Phase I trial in April 2009 and currently being evaluated in a Phase II trial for the treatment of rheumatoid arthritis initiated in September 2010.

Rheumatoid arthritis is a chronic inflammatory disease that leads to pain, stiffness, swelling and limitation in the motion and function of multiple joints. If left untreated, rheumatoid arthritis can produce serious destruction of joints that frequently leads to permanent disability. Though the joints are the principal body part affected by rheumatoid arthritis, inflammation can develop in organs and other body parts as well. The disease currently affects over two million Americans, almost 1% of the population, and is two to three times more prevalent in women. Onset can occur at any point in life with most patients developing the disease between the ages of 35 and 50.

Given the variation in the metabolism of MTX, we believe that our novel antifolates might have significant clinical advantages over MTX in rheumatoid arthritis patients due to metabolic stability. Because of this stability, it can be hypothesized that in those patients who fail to achieve a sufficient therapeutic response to MTX as a result of either a slower or more rapid metabolism of MTX, a non-metabolized antifolate might be clinically efficacious since it is not deactivated by these enzymatic processes.

#### *CH-4051*

In parallel to our clinical development of CH-1504, we continued additional preclinical evaluation, including formulation work on the enantiomers of CH-1504. After conducting studies to determine the relative potency of the L- and D-isomers, we found that the L-isomer, now identified as CH-4051, was the more potent of the two thus prompting additional preclinical evaluation of CH-4051.

In April 2008, we reported findings from a 17-day preclinical study of CH-4051 designed to test the efficacy of CH-4051 in a rat collagen-induced arthritis, or CIA, model. The results reveal efficacy in delaying the onset of the disease, significantly decreasing the severity and, at certain doses, completely blocking all development of rheumatoid arthritis. The most significant finding from this study was that once daily dosing of 10mg/kg of CH-4051 administered from day 0 completely prevented the onset of arthritis. Similarly, twice daily 5mg/kg doses of CH-4051 reduced the severity of disease in all animals and prevented disease onset in some. Both the once-daily dose of 10mg/kg and the twice-daily dose of 5mg/kg dose of CH-4051 demonstrated better prevention of disease than 0.25mg/kg of methotrexate (a known maximally tolerated dose, or MTD, in this model) administered every three days.

In April 2009, we announced positive findings from our Phase I study of CH-4051. Data from this single and multiple ascending dose study demonstrated that CH-4051 is safe and well tolerated up to a MTD of 7.5mg. This randomized, double-blind, placebo-controlled study was conducted at Kendle International's Clinical Pharmacology Unit in the Netherlands. The primary objective of the study was to evaluate the safety, tolerability and pharmacokinetics of single and multiple ascending doses of CH-4051 in healthy male volunteers and to determine the MTD.

The single ascending dose, or SAD, phase of the study evaluated 5mg, 10mg, 20mg and 40mg doses of CH-4051. Each group contained 6 volunteers randomized 5:1 to receive either CH-4051 or placebo. In this escalating dose study, each cohort of subjects received a higher dose of the drug than the preceding cohort.

Based on the findings from the SAD study, we selected 5mg, 7.5mg, 10mg and 20mg of CH-4051 for evaluation in a multiple ascending dose, or MAD, study with the objective of exploring a wide range of doses,

including and exceeding those believed to be therapeutically relevant. In the MAD study, 32 subjects in 4 cohorts of 8 volunteers were randomized 6:2 to receive repeat daily oral doses of CH-4051 or placebo for 14 consecutive days.

Results demonstrated that CH-4051 was well tolerated at doses up to and including 7.5mg, a dose range likely to be effective for multiple autoimmune disorders. The 5mg dose was as well tolerated as placebo. High doses of CH-4051 demonstrated mostly mild toxicities, with the 10mg and 20mg doses groups reporting both gastrointestinal side-effects and reversible liver enzyme elevations. No serious adverse events occurred during the study. The dose range determined to be safe and well tolerated in this study is substantially higher than the 0.25mg to 1mg dose range of the less potent CH-1504 that demonstrated comparable efficacy and improved safety and tolerability to methotrexate in the recent Phase II rheumatoid arthritis trial.

Based on these findings, we initiated a double-blind, multiple-arm randomized Phase II study, with a primary efficacy endpoint of the American College of Rheumatology, or ACR, hybrid score that combines a continuous scale of percentage improvement with the well-known ACR20/50/70, in September 2010.

#### *CH-1504*

In June 2005, we commenced Phase I single and multiple dose escalation clinical trials of CH-1504 in healthy volunteers. These trials were conducted at Guy's Hospital in London under the Clinical Trial Authorization, issued by the Medicines and Healthcare Products Regulatory Agency, the United Kingdom's health authority. The in vivo portion and preliminary analysis of these trials were completed in December 2005.

Continuing evaluation of these results in light of additional preclinical data suggested that the bioavailability of CH-1504 was low and had significant pharmacokinetic variability. Following a review of available data suggesting the bioavailability of our free-acid formulation of CH-1504 could be improved, we reformulated CH-1504 utilizing a disodium-salt formulation. Subsequent human bioequivalence studies showed 1mg of the new formulation to be comparable to 15mg of the original free-acid formulation and demonstrated an 11.4-fold improvement in relative bioavailability, as measured by area under the curve with an 8.9-fold increase in peak plasma levels (C<sub>max</sub>).

In March 2009 we announced the results of a Phase II proof of concept study for CH-1504 in rheumatoid arthritis. The study was a multi-national, 12-week double-blind and randomized study in Russia, Ukraine, Poland and Canada with 200 MTX-naïve rheumatoid arthritis patients. The 4-arm trial included a 0.25mg, 0.5mg or 1mg daily dose of CH-1504 versus a 20 mg weekly dose of MTX. Results showed comparable ACR 20/50/70 response rates among patients treated with CH-1504 compared to methotrexate. In addition, the efficacy of CH-1504 was associated with improved tolerability and reduced liver enzyme elevations compared with methotrexate.

Because Phase I data suggests CH-4051 retains the superior safety and tolerability profile of CH-1504 while preclinical data suggests both an enhanced potency compared to CH-1504 and significant superiority to methotrexate, we have no additional trials planned for CH-1504.

#### **Other Potential Indications for our Antifolate Portfolio**

As we proceed in our clinical development of our antifolate portfolio for rheumatoid arthritis, we expect to continue our evaluation of its potential in other indications. Additional potential indications for our antifolates include rheumatoid arthritis, psoriasis, Crohn's disease, uveitis, ankylosing spondylitis, inflammatory bowel disease, certain cancers and other immunological disorders. If and as our antifolates advance in rheumatoid arthritis studies, we will begin to focus on the timing of clinical programs for our antifolate compounds in these additional indications. Notwithstanding the foregoing, because of our limited funding, clinical studies will initially be pursued in rheumatoid arthritis.

## Antifolate Competition

There are many different drugs that are used to treat rheumatoid arthritis, including hormones, small molecules and biologics, which are manufactured using recombinant technology. The normal course of therapy for rheumatoid arthritis begins with analgesics, such as aspirin, and non-steroidal anti-inflammatory agents, followed by disease modifying anti-rheumatic drugs, or DMARDs, including low dose steroids, MTX, dihydroorotate dehydrogenase, or DHODH, inhibitors and biologics, and, finally, reconstructive joint surgery for patients failing all therapies. DMARDs are the only drugs that have been shown to alter the course of the disease.

*Currently Available Antifolates.* MTX, a classical antifolate, was originally used as a chemotherapy drug to treat certain kinds of cancer, but was also found to be beneficial in treating inflammatory arthritis and psoriasis. MTX is generic and marketed in both injectable and oral formulations by multiple companies including Barr Laboratories, Boehringer Ingelheim Pharma, Mayne Pharma and Mylan Laboratories. Traditional oral DMARDs include MTX, leflunomide, auranofin, sulfasalazine, cyclosporine, hydroxychloroquine, azathioprine and penicillamine.

*Currently Available Biologics.* Although there have been positive results for biologics, we believe physicians are likely to reserve anti-tumor necrosis factor, or anti-TNF, and other biologic therapies for patients who have failed or had a limited response to initial MTX monotherapy. Despite increased aggressiveness of treating physicians and easier reimbursement, we believe front line use with biologics either in monotherapy or in combination with MTX is unlikely to occur due to their high costs and side effect profile. Enbrel<sup>®</sup>, Humira<sup>®</sup> and Remicade<sup>®</sup> are TNF blockers that have been approved by the FDA and are the top selling biologics for rheumatoid arthritis. These three TNF blockers are administered to patients by injection and can be used alone or in combination with other DMARDs, such as MTX, or NSAIDs such as aspirin or ibuprofen.

Enbrel<sup>®</sup>, which is developed by Amgen, is the top selling biologic for rheumatoid arthritis, and is also indicated for juvenile rheumatoid arthritis, early rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. Enbrel<sup>®</sup> had global sales of \$6.3 billion in 2009. Remicade<sup>®</sup> is a chimeric anti-TNF monoclonal antibody developed by Johnson & Johnson for the treatment of rheumatoid arthritis and Crohn's disease with combined global sales of \$4.4 billion in 2009. Abbott Laboratories' Humira<sup>®</sup> had 2009 global sales of \$5.4 billion. Both Remicade<sup>®</sup> and Humira<sup>®</sup> contain black box warnings for tuberculosis. Rituxan<sup>®</sup>, an anti-CD20 monoclonal antibody, is currently marketed by Genentech and Roche for rheumatoid arthritis in patients refractory to other DMARD therapy. Orencia<sup>®</sup> (abatacept), a CTLA-4 fusion protein, developed by Bristol-Myers Squibb, is marketed as a once-monthly infusion for rheumatoid arthritis as a monotherapy and combination with sales of \$0.6 billion in 2009. UCB is currently marketing Cimzia<sup>®</sup>, an injectable, pegylated anti-TNF antibody for the treatment of rheumatoid arthritis in the United States with sales of \$104 million in 2009.

*DMARDs in Development.* Rigel Pharmaceuticals' R788 (fostamatinib disodium), licensed by AstraZeneca in February 2010, showed proof of concept in a Phase II clinical trial in rheumatoid arthritis. An oral syk kinase inhibitor, R788 demonstrated statistically significant results in treating rheumatoid arthritis patients. Pfizer is in Phase III development of an oral tablet formulation of CP-690550 (tasocitinib), a Janus kinase (JAK)-3 inhibitor, for the potential treatment of rheumatoid arthritis, psoriasis, asthma and inflammatory bowel disorders, including Crohn's disease and ulcerative colitis, and the treatment of transplant rejection. We believe that with significant ACR scores and good tolerability as observed in clinical trials to date, and with the benefit of oral delivery, R788 and CP-690550 may be favorable alternatives to the currently approved biological agents. However, we anticipate that, like other biologics, these compounds would work best in combination with MTX or similar antifolates and should not significantly impact the opportunity available to our antifolate portfolio.

## Antifolate Marketing

Given the size of the rheumatoid arthritis market, the vast sales forces required to compete in this market, and the necessary infrastructure required, our marketing strategy for our antifolates is likely to include

contracting with or licensing to third parties, particularly for territories outside the United States. It is possible that we might directly commercialize or co-promote our antifolate compounds in the smaller therapeutic indications such as psoriasis or irritable bowel disease. Out-licensing arrangements might be negotiated and entered into prior to one or more of our antifolate drug candidates being approved for marketing.

## **I-3D PORTFOLIO**

### **Overview**

In May 2006, we signed an agreement with Active Biotech AB for the co-development and commercialization of the I-3D portfolio, a group of orally active compounds that inhibit the enzyme DHODH for the treatment of autoimmune diseases and transplant rejection. At the time of the agreement, Active Biotech had already isolated more than 15 compounds and conducted extensive preclinical modeling resulting in the identification of two potential lead compounds.

Having previously demonstrated proof of concept in both rheumatoid arthritis and transplant rejection in animal models, the joint development committee selected AB-224050 as the first I-3D compound to undergo IND-enabling toxicology studies during the third quarter of 2006. As part of the ongoing evaluation and preparation for Phase I trials, the joint development committee initiated a Phase 0 (micro-dosing) study to evaluate the half-life of AB-224050 in humans in the first quarter of 2007. Based on the results of the micro-dosing study and other ongoing preclinical activity, it was determined that, while demonstrating a significantly shorter half-life than Arava®, AB-224050 would require additional work prior to the commencement of Phase I clinical trials. In 2007, the joint development committee continued preclinical optimization of AB-224050 and conducted further comparisons of AB-224050 versus other compounds in the I-3D.

In April 2008, following a decision to focus its resources on its immunomodulatory compounds, Active Biotech AB discontinued its participation in the I-3D co-development program and granted us exclusive global rights to the portfolio in exchange for royalties on future sales. As a result of our limited funding and strategic development efforts associated with the development of droxidopa and our antifolate drug candidates, we currently do not have any active clinical or preclinical programs associated with compounds from this portfolio.

### **I-3D Additional Indications**

In addition to therapeutic applications in rheumatoid arthritis, compounds from the I-3D portfolio are believed to have broad clinical application in immune-mediated inflammatory disorders including transplant rejection, psoriasis and systemic lupus erythematosus.

### **Scientific Advisory Boards**

We retain the services of certain qualified individuals on our Scientific Advisory Boards which normally meet at least yearly. Meetings or consultations with Scientific Advisory Board members are held more often when significant developments arise or new information becomes available that require expert review. The boards provide an opportunity to review our scientific, research and clinical development plans from the perspective of experts and key opinion leaders in the medical community. Specifically, the Scientific Advisory Boards provide advice concerning the design of clinical research protocols to be utilized for the development of our drug candidates and they provide an opportunity to test the validity of our assumptions regarding the attitudes of the medical community relative to various drug characteristics that might be highlighted during development.

Our Scientific Advisory Board for NOH consists of the following individuals:

*Horacio Kaufmann, MD* is currently the F.B. Axelrod Professor of Neurology and Professor of Medicine and Pediatrics at the New York University School of Medicine. He is the Director of the Dysautonomia Research Laboratory at the New York University Medical Center. Dr. Kaufmann is the past President of the American

Autonomic Society, former Chairman of the Autonomic Nervous System Section of World Federation of Neurology and the American Academy of Neurology and co-Editor-in-Chief of Clinical Autonomic Research. He is a world renowned expert in the treatment of autonomic disorders, autonomic physiology and pathophysiology. Dr. Kaufmann has published extensively in the medical literature, particularly on the treatment of orthostatic hypotension in neurodegenerative disorders, such as Parkinson's disease and multiple system atrophy. His research on autonomic disorders has been funded by the National Aeronautics and Space Administration, the National Institute of Health, National Organization of Rare Disorders, the DANA foundation and the Dysautonomia Foundation.

*Roy Freeman, MD* is Professor of Neurology at Harvard Medical School and director of the Center for Autonomic and Peripheral Nerve Disorders in the Department of Neurology at Beth Israel Deaconess Medical Center in Boston, Massachusetts. Dr. Freeman's clinical and research expertise is in the physiology and pathophysiology of the autonomic nervous system and small nerve fibers. He is also an authority on the neurological complications of diabetes, the autonomic complications of Parkinson's disease and multiple system atrophy, the diagnosis and treatment of autonomic and peripheral nervous system disorders and neuropathic pain. Dr. Freeman is widely published in these research areas.

*Phillip Low, MD* is past chairman of the Division of Neurophysiology at the Mayo Clinic in Rochester, Minnesota. He is founder and director of the Autonomic Laboratory which evaluates autonomic function. He serves as Director of the Mayo Autonomic Disorders Project, the first program grant for autonomic disorders to be funded by the National Institutes of Health. His research is focused on studies of the pathophysiology of orthostatic intolerance and its amelioration. Diseases studied include multiple system atrophy, autoimmune autonomic neuropathy and postural tachycardia syndrome. Dr. Low is Associate Editor of the journal Autonomic Neuroscience. He also serves on the editorial board of numerous publications including Muscle & Nerve, Journal of Clinical Neurophysiology and Journal of Clinical Neuromuscular Diseases. He also serves on the scientific advisory board of the Neuropathy Association and is a member of the steering committee NIDDK/NHLBI Animal Models of Diabetic Complications Neuropathy Disease Validation Committee.

*Peter LeWitt, MD* is Professor of Neurology and Psychiatry at Wayne State University School of Medicine in Detroit, Michigan. He is a specialist in Parkinson's disease and other movement disorders and also directs a laboratory research program investigating neurochemical mechanisms and diagnostic markers in Parkinson's and Alzheimer's diseases. He has served as a scientific review consultant for the National Institutes of Health and the Veterans Administration. Other advisory affiliations with national organizations include the International Essential Tremor Foundation and the National Parkinson Foundation. Dr. LeWitt further serves as president of the Michigan Parkinson Foundation. He has been a steering committee member and clinical investigator for the Parkinson Study Group and other clinical trials research consortia. Dr. LeWitt is editor-in-chief of Clinical Neuropharmacology and also serves on the editorial board of the Journal of Neural Transmission.

*Italo Biaggioni, MD* is Professor of Medicine and Pharmacology and the Associate Director of the General Clinical Research Center, which he developed, at Vanderbilt University in Nashville, Tennessee. With over 25 years of experience in biomedical research in general and clinical research in particular, the focus of Dr. Biaggioni's clinical research is the interaction between neural (autonomic) and metabolic (adenosine, nitric oxide) factors that regulate blood pressure. His basic research focuses on the role of adenosine receptors in disease processes and their target for drug development. He has had 20 years of continuous funding from the National Institute of Health, over 200 publications in peer-reviewed journals, and is on the editorial board of several journals including *Hypertension*, *Journal of Pharmacology and Experimental Therapeutics*, *Journal of Applied Physiology and Clinical Autonomic Research*. He is a founding member of the American Autonomic Society and served as its President from 2006 to 2008.

Our Scientific Advisory Board for rheumatology consists of the following individuals:

*Lee Simon, M.D.* is presently a principal in a consulting firm helping companies to create successful drug development programs through good designs and using insightful regulatory strategy. He also serves as head

regulatory consultant to Leerink Swann/Medacorp in Boston, Massachusetts. He previously had served as a voluntary faculty member at Harvard and the Beth Israel Deaconess Medical Center and has been a rheumatologist for 25 years. Dr. Simon is a fellow of the American College of Physicians and the American College of Rheumatology. Dr. Simon received his M.D. from the University of Maryland, completed his internship and residency in internal medicine at the Johns Hopkins Hospital, and trained in the arthritis unit of the Massachusetts General Hospital and Harvard Medical School. In addition to his many academic appointments, Dr. Simon has been a consultant to and a senior member of the FDA where he served as Division Director for analgesic, anti-inflammatory and ophthalmologic drug products. Dr. Simon has served on the editorial boards of multiple journals, has authored more than 110 original publications, review articles, and chapters, and has served as an editor of four books.

*Vibeke Strand, M.D.* is an Clinical Professor in the Division of Immunology at Stanford University School of Medicine and has over twenty years of experience as a clinical investigator and subspecialist rheumatologist in private practice as well as in senior positions in pharmaceutical and biotechnology firms, planning and overseeing clinical trials in autoimmune diseases, AIDS, transplantation and cancer. For the past eleven years, she has served as an independent consultant in clinical and regulatory affairs to pharmaceutical and biotechnology companies, developing strategies for the efficient development of immunologically-based products and treatments for autoimmune diseases. She has worked to promote forums for the discussion of rational product development among industry, FDA and academia. She is a co-founder of a biyearly conference and a member of the organizing committees for six international consensus conferences on outcome measures for rheumatology clinical trials. As a fellow of the American College of Physicians and the American College of Rheumatology, she has authored or co-authored more than 75 articles, 20 book and textbook chapters and co-edited two books. Dr. Strand earned her M.D. at the University of California San Francisco School of Medicine. She completed a residency in Internal Medicine at Michigan State and a Fellowship in Rheumatology/Immunology at the University of California San Francisco School of Medicine.

*Arthur F. Kavanaugh, M.D.* is a Professor of Medicine at the University of California, San Diego (UCSD) School of Medicine. In addition, he is the Director of the Center for Innovative Therapy of the UCSD Division of Rheumatology, Allergy, and Immunology. Dr. Kavanaugh earned his BS in biology at the Massachusetts Institute of Technology in Cambridge, Massachusetts and his M.D. at Saint Louis University School of Medicine in Saint Louis, Missouri. He completed a residency in Internal Medicine and then a fellowship in Clinical Immunology/Allergy at the Baylor College of Medicine in Houston, Texas. Dr. Kavanaugh also completed a Rheumatology fellowship at the University of Texas Southwestern Medical School in Dallas. Dr. Kavanaugh has authored more than 120 scientific publications and book chapters. He is on the editorial board for several journals, and has served as peer reviewer for more than a dozen scientific journals. Dr. Kavanaugh is a fellow of the American Academy of Allergy, Asthma, and Immunology, and the American College of Rheumatology, or ACR. He has been a member of and chaired a number of committees in these organizations.

*Joel M. Kremer, M.D.* is a Professor of Medicine at the Albany Medical College and is also Director of Research at The Center for Rheumatology in Albany. Dr. Kremer earned his M.D. from Temple University School of Medicine and trained in Internal Medicine and Rheumatology at Albany Medical College. He has worked extensively with methotrexate and combinations of new agents with methotrexate. Dr. Kremer is the recipient of the Engalaticheff Award given by The Arthritis Foundation for “contributions which improve the quality of life of patients with arthritis” in 1997. He is the author of approximately 100 peer-reviewed publications, 16 chapters and six texts. He is president and founder of CORRONA, a research organization which gathers data from rheumatologists and patients throughout the United States.

*Michael H. Schiff, M.D.* is Clinical Professor of Medicine, Rheumatology Division, University of Colorado School of Medicine at Denver and is board certified in Internal Medicine and Rheumatology. Dr. Schiff has received a number of Outstanding Clinical Faculty awards from the University of Colorado School Of Medicine, including the Academic Publications Award and the Research Project Award and was recently awarded the University of Colorado Career Achievement Award 2006. He was a founder of the Denver Arthritis Clinic in

1976 where he practiced rheumatology and was the medical director of the clinical research unit until 2008. He has been principle investigator for over 200 research projects and has published 50 peer-reviewed journal articles and 200 scientific abstracts. Dr. Schiff is a fellow of the American College of Rheumatology, as well as a member of a number of regional and national medical societies. In addition, Dr. Schiff has served as a board member of the American College of Rheumatology's Research Education Foundation and served as vice president from 2001–2002. He served two terms as president of the Colorado Society of Internal Medicine. His primary interest has been in the use of DMARDs and biologics for the management of rheumatoid arthritis.

*Edward C. Keystone, M.D.* is a Professor of Medicine at the University of Toronto and a Senior Consultant in Rheumatology at Mount Sinai Hospital. Dr. Keystone recently established The Rebecca Macdonald Centre for Arthritis and Autoimmune Disease, which is devoted to research into genomics, therapeutics, and outcomes in autoimmune inflammatory joint disease. Dr. Keystone obtained his M.D. and specialty degrees and fellowships in both Rheumatology and Internal Medicine from the University of Toronto. He then carried out his research training at the Clinical Research Centre in Harrow, London, United Kingdom. He was on staff as a consultant rheumatologist at The Wellesley Central Hospital, Toronto from 1976 to 1998. He is the author of more than 145 peer-reviewed papers, reviews and book chapters, and has been the recipient of numerous teaching awards and honors, including the Senior Investigator Award of the Canadian Rheumatology Association.

### **Government Regulation**

The FDA and foreign regulatory agencies regulate many aspects of product development and marketing of our product candidates including research, development, manufacture, labeling, promotion, advertising, distribution, and marketing. Meeting the various U.S. and international regulatory requirements often takes several years, and the actual time required can vary substantially based upon the type, complexity and novelty of the pharmaceutical product and the therapeutic indication. Furthermore, meeting the regulatory requirements as well as maintaining compliance often necessitates implementing costly procedures. Failure to comply with the applicable requirements mandated by the FDA and other regulatory agencies can result in administrative or judicial sanctions. In the United States, such sanctions may include the FDA's refusal to approve pending NDAs, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions and/or criminal prosecution.

Success in preclinical or early-stage clinical trials does not ensure success in late-stage clinical trials. Data obtained from preclinical and early stage clinical activities are not always conclusive and are susceptible to varying interpretations that could negatively impact our trials and delay, limit or prevent regulatory approval. In addition, we cannot be certain that the FDA or any other international regulatory agency will grant approval for any of our products under development on a timely basis, if at all. Delays in obtaining, or failures to obtain, regulatory approvals would have a material adverse effect on our business. Even if a product receives regulatory approval, the approval might be significantly limited to specific indications or uses. After regulatory approval is obtained and the product becomes available on the market, the later discovery, over time, of previously unknown problems with a product might result in restrictions on the product or even complete withdrawal of the product from the market.

### *Drug Approval Process in the United States*

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and those regulations are published in the Federal Register. None of our drugs may be marketed in the United States until the drug has received FDA approval. The process required before a drug can be marketed in the United States includes:

- preclinical laboratory tests, animal pharmacology and toxicology studies, and formulation studies;
- submission to the FDA of an investigational new drug application, or IND, for human clinical testing, which must be cleared by the FDA before human clinical trials can begin in the United States;

- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each indication;
- submission to the FDA of a new drug application, or NDA;
- satisfactory completion of any FDA inspections of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practices, or cGMPs;
- FDA review and approval of the NDA; and
- the completion of any contingent requirements of the FDA as a condition to maintaining marketing approval once granted.

Preclinical tests include laboratory tests and animal studies. The conduct of the preclinical tests as well as the formulation of the compounds must comply with FDA regulations. The preclinical test data, together with manufacturing information and analytical data of product chemistry, are submitted to the FDA as part of an IND, which must become effective before human clinical trials can begin. Human clinical trials submitted to the FDA as part of an IND will automatically become effective 30 days after receipt by the FDA, unless, within that 30 days, the FDA raises concerns or questions regarding the clinical trials, or places a clinical hold on the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. We cannot be certain that submission of an IND will result in clearance by the FDA to allow clinical trials to begin.

Clinical trials involve the administration of the investigational drug to human subjects under the supervision of qualified clinical investigators. Clinical trials are conducted under protocols detailing the objectives of the study, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each clinical trial protocol must be submitted to the FDA as part of an IND.

Clinical trials typically are conducted in three sequential phases, but the phases might overlap. The study protocol and informed consent information for study subjects in clinical trials must also be approved by an Institutional Review Board for each institution where the trials will be conducted. Study subjects must sign an informed consent form before participating in a clinical trial. The normal clinical trial phases are:

- Phase I usually involves the initial introduction of the investigational drug into healthy volunteers to evaluate its short-term safety, dosage tolerance, metabolism, pharmacokinetics and pharmacologic actions, and, if possible, to gain an early indication of its effectiveness.
- Phase II usually involves trials in a small patient population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the drug for specific indications.
- Phase III trials usually involve further evaluation of clinical safety and efficacy by using the drug in its final form in a larger patient population.

There can be no assurance that Phase I, Phase II, or Phase III testing will be completed successfully within any specified period of time, if at all. Furthermore, clinical trials might be suspended by us or the FDA at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

Once the required clinical testing is successfully completed, the results of the preclinical studies and of the clinical studies, as well as information on the manufacture and composition of the drug, are submitted to the FDA in an NDA. If the FDA grants NDA approval, the product can then be marketed for one or more approved indications. On the other hand, if the FDA reviews the application and deems it to be inadequate to support the NDA approval, and hence, marketing approval, we cannot ensure that any approval will be granted on a timely basis, if at all. The FDA might also refer the application to the appropriate advisory committee, typically a panel of clinicians and scientists, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee.

The overall drug development process, including preclinical testing, clinical trials through to marketing approval requires substantial time, effort and financial resources.

The FDA has various programs, including fast track, priority review, and accelerated approval, that are intended to expedite or simplify the process for reviewing drugs, and/or provide for approval on the basis of surrogate endpoints. Generally, drugs that might be eligible for one or more of these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that provide meaningful benefit over existing treatments. We cannot ensure that any of our drugs will qualify for any of these programs, or that, if a drug does qualify, that the review time will be reduced.

Section 505b2 of the FDCA allows the FDA to approve a follow-on drug on the basis of data in the scientific literature or data used by FDA in the approval of other drugs. This procedure potentially makes it easier for generic drug manufacturers to obtain rapid approval of new forms of drugs based on proprietary data of the original drug manufacturer.

Before approving an NDA, the FDA usually will inspect the facility or the facilities at which the drug is manufactured, and may not approve the product unless the manufacturing site is good manufacturing practices, or cGMP, compliant. If the FDA evaluates the NDA and the manufacturing facilities as acceptable, the FDA might issue an approval letter, or in some cases, an approvable letter followed by an approval letter. Both letters usually contain a number of conditions that must be met in order to secure final approval of the NDA. When and if those conditions have been met to the FDA's satisfaction, the FDA will issue a final approval letter. The final approval letter authorizes commercial marketing of the drug for specific indications. As a condition of NDA approval, the FDA might require post-marketing testing and surveillance to monitor the drug's safety or efficacy, or they may impose other conditions.

After approval, certain changes to the approved product, such as adding new indications, making certain manufacturing changes, or making certain additional labeling claims, are subject to further FDA review and approval and may require the submission of a supplemental NDA. Before we could market our product candidates for additional indications, we must obtain additional approvals from the FDA. Obtaining approval for a new indication generally requires that additional clinical studies be conducted. We cannot ensure that any additional approval for new indications, if any, for any product candidate will be approved on a timely basis, or at all.

#### *Post-Approval Requirements*

Often, even after a drug has been approved by the FDA for sale, the FDA might require that certain post-approval requirements be satisfied, including the conduct of additional clinical studies. If such post-approval conditions are not satisfied, the FDA might withdraw its approval of the drug. In addition, holders of an approved NDA are required to:

- report certain adverse reactions to the FDA;
- comply with certain requirements concerning advertising and promotional labeling for their products; and
- continue to have quality control and manufacturing procedures conform to cGMP after approval.

The FDA periodically inspects the sponsor's records related to safety reporting and/or manufacturing facilities, including an assessment of compliance with cGMP. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. We intend to use third party manufacturers to produce our products in clinical and commercial quantities, and future FDA inspections might identify compliance issues at the facilities of our contract manufacturers that might disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product after approval might result in restrictions on a product, manufacturer, or holder of an approved NDA, including withdrawal of the product from the market.

### *Orphan Drug Designations*

The FDA can grant orphan drug designation to drugs intended to treat a rare disease or condition, which generally is a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. If the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are publicly disclosed by the FDA. Orphan drug designation does not necessarily convey an advantage in, or shorten the duration of, the review and approval process. If a product which has an orphan drug designation subsequently receives the first FDA approval for the indication for which it has such designation, the product is entitled to orphan exclusivity, meaning that the FDA will not approve any other applications to market the same drug for the same indication, except in certain very limited circumstances, for a period of seven years. Orphan drug designation does not prevent competitors from developing or marketing different drugs for that indication.

### *Regulations Outside the United States*

Before our products can be marketed outside of the United States, they are subject to regulatory approval similar to that required in the United States, although the requirements governing the conduct of clinical trials, including additional clinical trials that might be required, product licensing, pricing and reimbursement vary widely from country to country. No action can be taken to market any product in a country until an appropriate application has been approved by the regulatory authorities in that country. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In certain countries, the sales price of a product must also be approved. The pricing review period often begins after market approval is granted. Even if a product is approved by a regulatory authority, satisfactory prices might not be approved for such product.

In Europe, marketing authorizations may be submitted via a centralized, decentralized or mutual recognition approach (or at a national level). The centralized procedure is mandatory for the submission of high technology/biotechnology products, products with an orphan medicinal product designation, if filing for indications contained in such designation, and certain therapeutic areas of community interest. This procedure provides for the grant of a single marketing authorization that is valid in all European Union member states. It is optional for those products and indications deemed innovative and also to generic products where the originator product was authorized via a centralized procedure. The decentralized and mutual recognition procedures are available for those products not subject to a mandatory centralized procedure. There can be no assurance that the chosen regulatory strategy will secure regulatory approvals on a timely basis or at all.

### **Manufacturing**

We own no manufacturing facilities, quality control laboratories or warehouses for storage and distribution of our product candidates. We use third-party contractors for manufacturing drug substances under development. We also use contractors for preformulation, formulation and analytical development as well as manufacturing of drug products used for clinical studies. If any of our products are approved by the FDA for marketing, we plan to use third-party contractors for producing the commercial product. This strategy enables us to direct our financial resources to product development without devoting resources to the time and costs associated with building manufacturing plants and laboratories and we plan on continuing this strategy for the foreseeable future.

### **Intellectual Property**

We actively seek to obtain, maintain and enforce patent protection for our products, formulations, processes, methods and other proprietary technologies, preserve our trade secrets, and operate without infringing on the proprietary rights of other parties, both in the United States and in other key markets. Our goal is to obtain, where appropriate, the broadest intellectual property protection possible for our current product candidates, including CH-1504, CH-4051 and droxidopa, and any future product candidates and proprietary technologies through a combination of contractual arrangements and patents, both in the United States and other countries.

Our patent estate for the antifolate portfolio, including CH-1504 and CH-4051, includes two issued U.S. patents, one issued European patent, ten pending U.S. patent applications, two pending Patent Cooperation Treaty (PCT) patent applications and several related patent applications pending in countries outside the United States, including Europe and Japan. The issued U.S. patents are U.S. Patent No. 5,912,251, issued June 15, 1999 and entitled “Metabolically Inert Anti-Inflammatory and Anti-Tumor Antifolates,” and U.S. Patent No. 7,829,708, issued November 9, 2010 and entitled “Metabolically Inert Antifolates for Treating Disorders of Abnormal Cellular Proliferation and Inflammation.” The issued European patent is EP 1,062,209 issued May 13, 2009. Three of the pending U.S. patent applications are published as US 2008-0214585, 2009-0253719 and US 2009-0253720 and the remainder are unpublished patent applications. The pending applications are directed to compositions, methods of use and certain new antifolate compounds.

The issued U.S. and European patents cover our current product candidates, CH-1504 and CH-4051, as well as certain analogues, including claims to these compounds as compositions of matter, in pharmaceutical formulations and for use in treatment of certain diseases. The pending U.S. patent applications and international applications expand our proprietary position, claiming additional compounds and their uses as well as new uses of CH-1504. We plan to continue to strengthen our patent estate on our antifolate portfolio by filing and pursuing additional patents.

Our patent estate for droxidopa includes five pending U.S. patent applications and sixteen related patent applications pending in countries outside the United States, including Europe and Japan which are directed to pharmaceutical compositions comprising droxidopa and therapeutic methods of treatment using droxidopa. We plan to continue to strengthen our patent estate on droxidopa by filing and pursuing additional patents.

The patent estate for the I-3D portfolio includes U.S. Patent No. 7,074,831, issued July 11, 2006, related issued patents in Europe, China, New Zealand, South Africa and Mexico, as well as a pending U.S. patent application and a number of related patent applications pending in countries outside the United States.

Our success also depends upon the skills, knowledge and experience of our scientific and technical personnel, our consultants and advisors, as well as our licensors and contractors. To help protect our proprietary know-how and our inventions for which patents are unobtainable or difficult to obtain, we rely on trade secret protection and confidentiality agreements. To this end, it is our policy to require all of our employees, consultants, advisors and contractors to enter into agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

## **Employees**

We have attracted and retained a management team with core competencies and expertise in numerous fields, including manufacturing, research, clinical, regulatory, sales, marketing and business development. Our management and advisors are comprised of experienced pharmaceutical and biotechnology industry veterans and respected experts. We are led by our Chief Executive Officer, Dr. Simon Pedder, formerly Vice President, Pharmaceutical Business, Oncology at Hoffmann-La Roche Inc., who has over 20 years of senior pharmaceutical management experience, including drug development and business experience. During his time at Roche, Dr. Pedder was responsible for a number of global development programs, successful registrations and product launches.

At March 1, 2011, we had a total of 30 employees. We believe the relationships with our employees are satisfactory. We anticipate that we will need to identify, attract, train and retain other highly skilled personnel as we continue to develop our product candidates. Hiring for such personnel is competitive, and there can be no assurance that we will be able to retain our key employees or attract, assimilate or retain the qualified personnel necessary for the development of our business.

## Where you can find additional information

Our website address is [www.chelseatherapeutics.com](http://www.chelseatherapeutics.com). We make available free of charge through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports as soon as reasonably practicable after such material is electronically filed with or furnished to the SEC.

## Executive Officers of the Registrant

The following table sets forth the name, age and position of each of our executive officers as of March 2, 2011.

<u>Name</u>	<u>Age</u>	<u>Position</u>
Simon Pedder	50	President, Chief Executive Officer and Director
J. Nick Riehle	58	Vice President, Administration and Chief Financial Officer
William D. Schwieterman	53	Vice President, Chief Medical Officer
L. Arthur Hewitt	57	Vice President, Chief Scientific Officer
Keith Schmidt	60	Vice President, Sales and Marketing
Joseph Oliveto	43	Vice President, Operations
Michael J. Roberts	41	Vice President, Business Development

**Simon Pedder, Ph.D.—President, Chief Executive Officer and Director.** Dr. Pedder joined us from Hoffmann-La Roche Inc. in April 2004 where he was Vice President of Pharmaceutical Business, Oncology and an executive officer since February 2003. Prior to that he served as the Vice President, Drug Development at Shearwater Corporation from May 2001 until December 2002. Prior to that Dr. Pedder served in a number of positions at Hoffmann-La Roche, including as Director, Pharmaceutical Business, Pharmaceutical Development and Project Management from May 1994 until May 2001. While at Hoffmann-La Roche, Dr. Pedder was in charge of the development of Pegasys and Copegus, which have combined annual worldwide sales of over \$1 billion, and oversaw a number of successful NDAs. Dr. Pedder has his Ph.D. in Pharmacology from the College of Medicine at the University of Saskatchewan in Canada.

**J. Nick Riehle, MBA—Vice President, Administration and Chief Financial Officer.** Mr. Riehle has been our Vice President, Administration and Chief Financial Officer since July 2004. Prior to that he served as Chief Financial Officer at HAHT Commerce, Inc., a software company, from August 1996 until June 2003 and as an independent contractor from July 2003 until July 2004. Prior to that, Mr. Riehle served in various roles at Nortel Networks and IBM. Mr. Riehle has his Bachelor of Commerce from McGill University, his MBA from York University and earned a Certified Management Accountant (CMA) designation from Ontario, Canada.

**William D. Schwieterman, M.D.—Vice President, Chief Medical Officer.** Dr. Schwieterman joined the company as an employee and officer in October 2009 after serving for more than a year on our Board of Directors and several years as a consultant and member of our Scientific Advisory Board for rheumatology. He is a rheumatologist and board-certified internist who was formerly Chief of the Medicine Branch and Chief of the Immunology and Infectious Disease Branch in the Division of Clinical Trials at the FDA. In these capacities and others, Dr. Schwieterman spent 10 years at the FDA in the Center for Biologics overseeing a wide range of clinical development plans for a large number of different types of molecules. Dr. Schwieterman helped author the FDA's "Good Review Practices" for investigational products, and was instrumental in developing several guidance documents for the industry. Since leaving the FDA, he has acted as an independent consultant to biotechnology and pharmaceutical companies, focusing on clinical drug development and regulatory matters. He currently serves on the board of directors of OXiGENE, Inc., a publicly traded company, and Neumedics, Inc., a privately held drug development company. Dr. Schwieterman holds a B.S. and M.D. from the University of Cincinnati.

**L. Arthur Hewitt, Ph.D.—Vice President, Chief Scientific Officer.** Dr. Hewitt was named our Chief Scientific Officer in January 2010 after serving as our Vice President, Drug Development since May 2004. Prior to that he served as an independent contractor from January 2003 to May 2004, as Director of Scientific Affairs at Shearwater Corporation, a drug delivery company, from October 2002 until January 2003 and as Director of Scientific Affairs for Amgen Canada from July 1991 until November 2000. During his years at Amgen, Dr. Hewitt oversaw the approval of Neupogen, Stemgen and Infergen. Dr. Hewitt obtained his Ph.D. in Pharmacology from the Medical School at the University of Montreal.

**Keith Schmidt, MBA—Vice President, Marketing and Sales.** Mr. Schmidt has served as our Vice President, Marketing and Sales since July 2006. In February 2007, Mr. Schmidt became one of our executive officers. Prior to that he was President of his biotech consulting company, Tellico Pharma LLC from June 2005 and served as Vice President of Thomson Healthcare Advanced Therapeutics Communications, a medical education company, from February 2002 until May 2005. From 1996 until January 2002, Mr. Schmidt served as an International Business Leader for Hoffmann-La Roche where he developed and led the global sales and marketing launch efforts for Pegasys and Copegus. Mr. Schmidt earned a Bachelor of Science from South Dakota State University and an MBA from the University of San Francisco.

**Joseph Oliveto, MBA—Vice President, Operations.** Mr. Oliveto joined us in June 2008 following a two-year assignment as Executive in Residence at Pappas Ventures, a life sciences venture capital firm. Prior to Pappas Ventures, he served in a number of progressively senior positions at Hoffmann-La Roche, most recently as the Global Alliance Director for Roche's licensing organization. Previous experience at Roche includes clinical development, project management, manufacturing process improvement and global business. During his tenure, he played an integral part in the success of multiple NDA filings, developed comprehensive launch programs, including those for both Pegasys and Copegus, and closed multiple licensing deals. Mr. Oliveto obtained a BA in Chemistry and an MBA from Rutgers University.

**Michael J. Roberts, Ph.D.—Vice President, Business Development.** Dr. Roberts was named an officer of Chelsea in January 2010 after having served since August 2004 as Senior Director of Business Development. He joined us from Nektar Therapeutics where he was Director of Business Development for their Molecule Engineering technology. Prior to this, he was Manager of Biopharmaceutical Research at Shearwater Corporation where he lead and was successful in the development of preclinical drug candidates from initial stages of research through Phase I clinical study. Dr. Roberts obtained his Ph.D. in Materials Science from the University of Alabama in Huntsville and B.S. in Chemical Engineering from Pennsylvania State University.

#### **ITEM 1A. RISK FACTORS.**

This report contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed in this report. Factors that could cause or contribute to these differences include, but are not limited to, those discussed below and elsewhere in this report and in any documents incorporated in this report by reference.

***We currently have no product revenue and will need to raise additional capital to operate our business.***

To date, we have generated no product revenue. Until, and unless, we receive approval from the FDA and other regulatory authorities for our product candidates, we cannot sell our drugs and will not have product revenue. Currently, our primary product candidates are droxidopa and our antifolates portfolio, and none are approved by the FDA nor, with the exception of droxidopa which has Japanese approval, any other regulatory agency for sale. Therefore, for the foreseeable future, we will have to fund all of our operations and development expenditures from cash on hand, equity or debt financings, licensing fees and grants. 2010 operating expenses totaled approximately \$38 million, including non-cash items and we anticipate that 2011 operating expenses will be approximately \$64 million, including non-cash items and significant spending related to marketing and commercialization activities for Northera in the United States.

In order to fund operations and increase our cash reserves, we may seek to out-license our products or seek additional sources of financing and such opportunities might not be available on favorable terms, if at all. If we do not succeed in raising additional funds on acceptable terms, we might not be able to complete planned preclinical and clinical trials or obtain approval of any product candidates from the FDA and other regulatory authorities. In addition, we could be forced to discontinue product development, reduce or forego sales and marketing efforts, forego attractive business opportunities or curtail operations. Any additional sources of financing could involve the issuance of our equity securities, which would have a dilutive effect on our stockholders.

***We are not currently profitable and might never become profitable.***

We have a history of losses and expect to incur substantial losses and negative operating cash flow for the foreseeable future, and we might never achieve or maintain profitability. Even if we succeed in developing and commercializing one or more product candidates, we expect to incur substantial losses for the foreseeable future and might never become profitable. From inception through December 31, 2010 we had losses of \$132.9 million. We had net losses of \$37.3 million, \$25.8 million and \$35.1 million for the years ended December 31, 2010, 2009 and 2008, respectively. Actual losses will depend on a number of considerations, including:

- the pace of commercialization and marketing effort for droxidopa;
- the pace and success of preclinical development and clinical trials for droxidopa, antifolates and other product candidates;
- possible out-licensing of our product candidates;
- seeking regulatory approval for our various product candidates;
- discussions with regulatory agencies concerning the design of our clinical trials and/or the adequacy of prior trials for filing our NDA;
- our ability to identify and recruit patients into our clinical trials at costs consistent with our current estimates;
- the pace of development of new intellectual property for our existing product candidates;
- in-licensing and development of additional product candidates;
- implementing additional internal systems and infrastructure; and
- hiring additional personnel.

We also expect to experience negative cash flow for the foreseeable future as we fund our operating losses. As a result, we will need to generate significant revenue in order to achieve and maintain profitability. We might not be able to generate revenue or achieve profitability in the future and are unlikely to do so in the near term. Our failure to achieve or maintain profitability could negatively impact the value of our securities.

***We are a development-stage company and might not be able to commercialize any product candidates.***

We are a development-stage company and have not demonstrated our ability to perform the functions necessary for the successful commercialization of any product candidates. The successful commercialization of any product candidates will require us to perform a variety of functions, including:

- continuing to undertake preclinical development and clinical trials;
- participating in regulatory approval processes;
- formulating and manufacturing products; and
- conducting sales, marketing and distribution activities.

Our operations have been limited to organizing and staffing our company, negotiating in-licensing agreements with our partners, acquiring, developing and securing our proprietary technology, participating in regulatory discussions with the FDA, the EMA and other regulatory agencies and undertaking preclinical trials and clinical trials of our product candidates. These operations provide a limited basis for you to assess our ability to commercialize our product candidates and the advisability of investing in our securities.

***Our potential future earnings may be reduced should we decide to out-license one or more of our drug product candidates.***

We may decide to out-license one or more of our drug product candidates, reducing future profits available to us. Should we license our drug product candidates to another pharmaceuticals company, it would allow the partner to market and sell our compounds in one or more markets around the world. If either the antifolates or droxidopa are licensed to a strategic partner, the profit available to us may be substantially reduced from what might otherwise be possible should we retain all rights to the products and market and sell them directly.

***We might not obtain the necessary U.S. or worldwide regulatory approvals to commercialize any product candidates.***

We cannot assure you that we will receive the approvals necessary to commercialize our product candidates including droxidopa, our antifolates, or any other product candidate either currently in our drug candidate portfolio or which we might acquire or develop in the future. We will need FDA approval to commercialize our product candidates in the United States and approvals from equivalent regulatory authorities in foreign jurisdictions to commercialize our product candidates in those jurisdictions. In order to obtain FDA approval of any product candidate, we must submit to the FDA an NDA demonstrating that the product candidate is safe for humans and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as preclinical studies, as well as human tests, which are referred to as clinical trials. Satisfaction of the FDA's regulatory requirements typically takes many years, depends upon the type, complexity and novelty of the product candidate and requires substantial resources for research, development and testing. We cannot predict whether our research and clinical approaches will result in drugs that the FDA considers safe for humans and effective for indicated uses. The FDA has substantial discretion in the drug approval process and may require us to conduct additional preclinical and clinical testing or to perform post-marketing studies. The approval process might also be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals might:

- delay commercialization of, and our ability to derive product revenue from, a product candidate;
- reduce available time during which our intellectual property is protected under various U.S. and foreign patents;
- impose costly procedures on us; and
- diminish any competitive advantages that we might otherwise enjoy.

Even if we comply with all FDA requests, the FDA may ultimately reject one or more of our NDAs. We cannot be sure that we will ever obtain regulatory clearance for any of our product candidates. Failure to obtain FDA approval of product candidates, particularly droxidopa or our antifolates, will severely undermine our business and could substantially extend the period before we have a saleable product, leaving us without any source of revenue until another product candidate can successfully be developed and commercialized. There is no guarantee that we will ever be able to develop and commercialize or acquire another product candidate or to obtain approval for any such additional product candidate that might be acquired.

In foreign jurisdictions, we must receive approval from the appropriate regulatory authorities before we can commercialize any drugs. Foreign regulatory approval processes generally include all of the risks associated with the FDA approval procedures described above. We cannot assure you that we will receive the approvals necessary to commercialize product candidates for sale outside the United States.

***Although the FDA has agreed to review our NDA based on Studies 301 and 302, there is no guarantee that we will obtain approval on this basis.***

On December 1, 2010, we completed a pre-NDA assessment meeting with the FDA. During that meeting, the FDA agreed that our proposed NDA for Northera could be submitted based on combined data from our two completed Phase III studies of Northera in NOH, Study 301 and Study 302. The FDA also agreed that results from Study 306, an additional Phase III study added at the recommendation of the FDA during a meeting held during the fourth quarter of 2009, would not be required as part of the integrated summary of efficacy for the indication claimed in the filing. Despite these positive developments related to our anticipated filing of an NDA for Northera, we cannot be certain that the FDA will approve our NDA submission in the timeframe anticipated, if at all, and we continue to face risks related to our Phase III registration program for Northera.

On February 2, 2011 we announced that an interim analysis of Study 306 indicated that further recruiting into this study was likely to be futile with respect to the primary endpoint of the study, namely, the orthostatic hypotension questionnaire composite scores, or OHQ composite. Subsequently we unblinded these 51 patients (now designated as the Study 306a population) and determined that favorable trends were seen in secondary indications including falls, OHQ Item 1 (dizziness), the Movement Disorder Society sponsored revised version of the Unified Parkinson's Rating Scale, or MDS-UPDRS, and Hoehn Yahr scores. We believe that these favorable trends, particularly in the objective endpoint of falls, are supportive of prior study results related to symptomatic endpoints. The failure to produce favorable results in the OHQ composite is not necessarily believed to be contradictory to prior studies due to differences in the characteristics of the specific populations and the length of the study treatment period. Nonetheless, we cannot predict whether the FDA will agree with this assessment. Specifically:

- the FDA may determine that approval cannot be granted for NOH in PD or in any other indications without additional studies. As a minimum, this could require us to delay filing until results for the remaining 306 patients (designated as Study 306b patients) are available, which are currently anticipated in the second quarter of 2012.
- although we plan to change the Study 306b primary endpoint to falls and although this endpoint trended favorably in 306a patients, there is no guarantee that the FDA will accept this as an appropriate endpoint for symptomatic NOH should they require an additional study for our NDA filing, nor that the results for the Study 306b population will show statistical significance in this endpoint.
- the targeted geographic distribution of patients as well as the targeted patient indication in Study 306b are different than in Study 302 and Study 301 and we cannot be certain that we will be able to meet our timeline for this study, particularly with respect to patient recruitment. While the pace of recruitment for Study 306a and Study 306b patients has been acceptable, we anticipate that with many of the available patients from identified study centers already enrolled in the 306 program, the pace of recruitment may slow as we attempt to recruit the remaining patients.
- even if the FDA agrees to evaluate our NDA without 306 data, the results of that review remain uncertain. While we believe that the design, performance and results of Study 302 and Study 301 are adequate to meet the FDA's expectations, we cannot be certain that the FDA will reach the same conclusion. Specific challenges related to the review by the FDA unrelated to the interim results of Study 306 include:
  - differences among geographic regions or among specific sites that the FDA might determine to be significant in evaluating Northera;
  - our reliance upon and the quality of oversight by third-party researchers in the completion of these trials and the FDA's review of the data quality results from the trials;
  - the quality, content and completeness of our NDA application; and
  - our inability to predict the outcome of the required QTc prolongation study and the inclusion of top-line data from that study at the time of the 90-day safety update.

- the completion and submission of an agreed-upon post-marketing study to evaluate the clinical pharmacology of Northera in renally-impaired patients, or other post marketing requirements that may result from the NDA review process, might adversely impact our label or even require withdrawal of Northera from the market should approval be obtained.
- any program delays resulting from the risks as outlined above might require additional financing for the droxidopa clinical program. If we require additional capital for the continued development of droxidopa, we may not be able to raise capital on favorable terms or at all. If such financing is equity financing it would cause dilution for our stockholders which could be significant depending on the price and the amount of stock sold.
- we may determine that it is in our best interest to out-license droxidopa. However, given the regulatory and financing uncertainties, we may not be able to complete an out-licensing agreement on terms beneficial to us or at all.

***We have not determined any additional requirements that may be needed in order to meet the expectations of the European Medicines Agency, or EMA, or other foreign regulatory agencies in order to obtain marketing approval for Northera outside the United States.***

Since an initial discussion several years ago, we have not conducted further discussions of the specifics of our clinical program with the EMA and we do not know if our current program will be acceptable for approval in Europe. While we continue to believe that the safety data from Study 306b with an extended period of placebo control will better meet the requirements as expressed by the EMA previously, this data will now be delayed until the second quarter of 2012, thus delaying the EMA filing until at least that timeframe. We intend to initiate discussions to better understand the EMA's expectations with regard to their efficacy requirements as well as to confirm the suitability of Study 306b safety data. However, until we have those discussions we will not be clear that the existing Study 301 and Study 302 data will be sufficient and if not, whether Study 306b data, with falls as a primary endpoint, will be adequate to complete the efficacy package. If not, we may be required to conduct additional efficacy trials and regardless, we cannot guarantee that Study 306b data will show a significant symptomatic benefit for patients with NOH or that any subsequent trials will provide adequately favorable data.

***Our product candidate CH-4051 has had only limited formal clinical trials.***

Our product candidate CH-4051 is in an early stage of development and requires extensive clinical testing. In November 2008, we commenced Phase I dose escalation clinical trials of CH-4051 in humans in Kende International's Clinical Pharmacology Unit, Utrecht, Netherlands under the authority of Stichting Therapeutische Evaluatie Geneesmiddelen—Medisch Ethische Toetsingscommissie, an Independent Ethics Committee. We initiated patient enrollment in our Phase II clinical trials for CH-4051 in rheumatoid arthritis in September 2010. We currently intend to seek a partner to assist us in the development of CH-4051 and our portfolio of antifolates after the completion of Phase II proof-of-concept studies for CH-4051 in rheumatoid arthritis. After the completion of those trials and depending on available funding, we may also initiate additional Phase II studies in rheumatoid arthritis and other indications as appropriate. We currently estimate a global filing of the NDA no sooner than 2013. However, at any point during the process we might decide to focus our efforts on a different lead compound, and we cannot predict with any certainty the success or timing of our clinical trials, if or when we might submit an NDA for regulatory approval of this product candidate or whether such an NDA will be accepted. We do not expect to conduct additional trials or make further investments in the development of CH-1504, formerly our lead antifolate product candidate.

***There has been only very limited testing of our I-3D product candidates.***

Our I-3D product candidates are early in their development. None of the candidates have had adequate toxicology testing in animals to permit clinical testing and there is no clinical evidence of efficacy for any of these candidates, despite limited similarities with compounds currently marketed by others. Animal toxicology

trials on our I-3D compounds may not permit further development of these drugs or we may have to carry out toxicology trials on several compounds before we find one that is appropriate for clinical testing, if at all. Once clinical trials are undertaken, the compound or compounds may not prove adequately safe and efficacious in humans and may not be approved by the FDA or other regulatory agencies. Moreover, because of the scarcity of capital and competing priorities within our development program we do not know when we will be able to continue any such testing or commence clinical trials.

***Clinical trials are very expensive, time-consuming and difficult to design and implement.***

Human clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial process is also time-consuming. For example, because we did not receive orphan drug status from the EMA for droxidopa as a treatment for Parkinson's disease, our clinical trials for that indication might have to be more involved and take longer to complete and get reviewed than otherwise would have been the case. Furthermore, failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon or repeat clinical trials. The commencement and completion of clinical trials might be delayed by several factors, including:

- unforeseen safety issues;
- clarification of dosing issues;
- lack of effectiveness during clinical trials;
- slower than expected rates of patient recruitment, including approximately 375 patients remaining to be recruited as of February 25, 2011, of the aggregate of approximately 615 patients required to complete the several Phase II and Phase III trials that are or are expected to be ongoing in 2011;
- inability to monitor patients adequately during or after treatment;
- inability or unwillingness of medical investigators to follow our clinical protocols; and
- unexpected emergence of competitive drugs against which our compounds might compete for clinical trial resources or need to be tested.

In addition, we or the FDA or another governing regulatory agency may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if the regulatory agency finds deficiencies in the conduct of these or our regulatory submissions. Therefore, we cannot predict with any certainty the schedule for our current or any future clinical trials.

***The results of our clinical trials might not support our product candidate claims.***

Even if our clinical trials are completed as planned, we cannot be certain that their results will support our product candidate claims. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and preclinical testing. The clinical trial process might fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. This failure would cause us to abandon a product candidate and might delay development of other product candidates. Any delay in, or termination of, our clinical trials will delay the filing of our NDAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenue.

***We intend to explore additional indications for droxidopa, however these programs may not prove successful.***

We have announced our exploration of certain additional indications for droxidopa and we may make similar announcements in the future. While trials conducted by our partner DSP for the Japanese market provide evidence of efficacy for certain indications, other indications may be explored for which we have no existing

clinical evidence of efficacy. Such trials are likely to be very costly. We do not have market approval from the FDA or other regulatory agencies for any of the indications we are exploring and there are no guarantees that additional clinical trials will provide new evidence of efficacy in the targeted indications or permit us to gain market approval from regulatory agencies.

***Physicians and patients might not accept and use our drugs.***

Even if the FDA approves any of our product candidates, physicians and patients might not accept and use them. Acceptance and use of our products will depend upon a number of factors including:

- perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our drug;
- cost-effectiveness of our product relative to competing products;
- understanding by prescribing physicians of the medical conditions we are attempting to address;
- availability of reimbursement for our product from government or other healthcare payers; and
- effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any.

Because we expect that sales of our product candidates could, if approved, generate a substantial portion of our product revenue for an extended period, the failure of such a drug to find market acceptance would harm our business and could require us to seek additional financing or curtail our operations.

***Our drug development program depends upon third-party researchers who are outside our control.***

We depend upon independent clinical research organizations, investigators and other collaborators, such as universities and medical institutions, to conduct our preclinical and clinical trials under agreements with us. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs. They might not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our drug development programs, if their performance is substandard or the FDA determines there are issues upon review of the study data, the approval of our FDA applications, if any, and our introduction of new drugs, if any, will be delayed. If we cannot successfully enter into new agreements with outside collaborators on acceptable terms, or if we encounter disputes over or cannot renew or, if necessary, amend existing agreements, the development of our drug candidates could be delayed. These collaborators might also have relationships with other commercial entities, some of which might compete with us. If our collaborators assist our competitors at our expense, our competitive position would be harmed.

***Our drug development program also depends upon our partners who are outside our control.***

We have licensed certain rights related to droxidopa from DSP and depend upon them for data and support in advancing our clinical program for this compound. In addition, DSP is currently the preferred manufacturer of this compound for our clinical program and commercialization efforts. Without the timely support of DSP or any other partners, our drug development programs could suffer significant delays, require significantly higher spending or face cancellation.

***We rely exclusively on third parties to formulate and manufacture any product candidates.***

We have only limited experience in drug formulation and no experience in drug manufacturing and do not intend to establish our own manufacturing facilities. We lack the resources and expertise to formulate or manufacture our own product candidates. While we have a contract in place with DSP covering droxidopa, we

currently have no contract for the commercial scale manufacture of our antifolates or I-3D compounds. We have contracted with one or more manufacturers to manufacture, supply, store and distribute drug supplies for our clinical trials. If any of our current product candidates or any other product candidates that we may develop or acquire in the future receive FDA approval, we will rely on one or more third-party contractors to manufacture our drugs. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to the following risks:

- We might not be able to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must approve any replacement contractor. This 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 products after receipt of FDA approval, if any.
- Our third-party manufacturers might be unable to formulate and manufacture our drugs in the volume and of the quality required to meet our clinical needs and commercial needs, if any.
- Our contract manufacturers might not perform as agreed or might not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store and distribute our products.
- Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration, or DEA, and corresponding state agencies to ensure strict compliance with good manufacturing practice and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.

Each of these risks could delay our clinical trials, the approval, if any, of our product candidates by the FDA or the commercialization of our product candidates or result in higher costs or deprive us of potential product revenue.

***We have limited experience selling, marketing or distributing products and only limited internal capability to do so.***

We currently have limited sales, marketing or distribution capabilities other than as provided by our Vice President of Sales and Marketing and several recent personnel additions in this area. As of December 31, 2010, we anticipate continued expansion of our marketing, sales and operational capabilities over the next 12 to 18 months in anticipation of commercializing droxidopa. We would need to allocate resources to, or contract with one or more third parties for, the sale and marketing of our other proposed products. As a result, our future success depends, in part, on our ability to enter into and maintain collaborative relationships or develop internal resources for these capabilities, either through hiring additional personnel, out-licensing our compounds or contracting for services from third-party providers.

To the extent that we decide not to, or are unable to, enter into collaborative arrangements with respect to the sales and marketing of our proposed products or if we decide to add internal resources to complement third party resources, significant development, expenditures, management resources and time will be required to establish and develop our own marketing and sales force with technical expertise.

***While the FDA has announced it might seek to remove midodrine from the market, we can have no assurances that it will be removed.***

In August 2010, the FDA proposed removing midodrine from the market because required post-approval studies to verify the clinical benefit of the drug have not been done by the manufacturer. However, in September, the FDA announced that it will not seek immediate removal and that the drug will be available for at least several months pending further review, particularly with Shire Pharmaceuticals, the holder of market approval for

midodrine. Further, in January 2011, the FDA announced the opening of a public docket to provide a forum to facilitate communication regarding the conduct of clinical trials needed to support the continued marketing authorization for midodrine. Midodrine is the only approved compound for orthostatic hypotension in the U.S. and its removal could facilitate higher sales and/or more rapid acceptance of Northera™ (droxidopa) in this indication. However, the FDA has never removed a drug under similar circumstances and we can provide no assurance that they will do so in the case of midodrine.

***If we cannot compete successfully for market share against other drug companies, we might not achieve sufficient product revenue and our business will suffer.***

The market for our antifolate product candidates is characterized by intense competition and rapid technological advances. The initial market for droxidopa, while smaller, has well established generic competition. Other markets for droxidopa, such as fibromyalgia, are emerging with new and heavily marketed offerings. If our antifolates, droxidopa or other product candidates receive FDA approval, they will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products might provide greater therapeutic convenience, efficacy or other benefits for a specific indication than our products or might offer comparable performance at a lower cost. If our products fail to capture and maintain market share, we will not achieve sufficient product revenue and our business will suffer.

We will compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have compounds already approved or in development. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs or have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- undertaking preclinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals of drugs;
- formulating and manufacturing drugs;
- launching, marketing and selling drugs; and
- post-marketing safety surveillance.

***Our ability to generate product revenue will be diminished if our drugs sell for inadequate prices or patients are unable to obtain adequate levels of reimbursement.***

Our ability to commercialize our drugs, alone or with collaborators, will depend in part on the extent to which reimbursement will be available from:

- government and health administration authorities;
- private health maintenance organizations and health insurers; and
- other healthcare payers.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Healthcare payers, including Medicare, are challenging the prices charged for medical products and services. Government and other healthcare payers increasingly attempt to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs. Even if a product candidate is approved by the FDA, insurance coverage might not be available and reimbursement levels might be inadequate to cover our drug. If government and other healthcare payers do not provide adequate coverage and reimbursement levels for our product, once approved, market acceptance and our revenue could be reduced.

Specifically, not all physicians recognize a separate indication for symptomatic neurogenic orthostatic hypotension and we cannot provide assurances that reimbursement will be approved by the relevant decision makers even if droxidopa receives market approval from the FDA or other regulatory authorities.

In addition, the U.S. and international healthcare industry is subject to changing political, economic and regulatory influences that may significantly affect the purchasing practices and pricing of pharmaceuticals. The laws and regulations governing and issued by the FDA and other healthcare policies might change, and additional government regulations might be enacted, which could prevent or delay regulatory approval of our product candidates. In March 2010, the U.S. Congress passed landmark healthcare legislation. We cannot predict what impact on federal reimbursement policies this legislation will have in general or on our business specifically. We anticipate that the U.S. Congress and state legislatures will continue to review and assess this legislation and possibly alternative health care reform proposals. The U.S. Congress may adopt additional legislation that could have the effect of putting downward pressure on the prices that pharmaceutical and biotechnology companies can charge for prescription drugs, including the proposed healthcare reform legislation. Cost-containment measures, whether instituted by healthcare providers or imposed by government health administration regulators or new regulations, could result in greater selectivity in the purchase of drugs. As a result, healthcare payers might challenge the price and cost effectiveness of our products. In addition, in many major markets outside the United States, pricing approval is required before sales may commence. As a result, significant uncertainty exists as to the reimbursement status of approved healthcare products.

***Developments by competitors might render our products or technologies obsolete or non-competitive.***

Companies that currently sell both generic and proprietary compounds for the treatment of rheumatoid arthritis include, but are not limited to, Abbott Laboratories, Amgen, Sanofi-Aventis, Barr Laboratories, Boehringer Ingelheim Pharma, Hoffmann-La Roche, Johnson & Johnson, Bristol-Myers Squibb, Mylan Laboratories and UCB. Alternative technologies are being developed to treat rheumatoid arthritis by numerous companies including Pfizer, Rigel, Astra Zeneca and GSK which are in advanced clinical trials or filed with regulatory agencies. Companies that currently sell compounds used for the treatment of orthostatic hypotension include Shire, Mylan Pharmaceuticals, Eon Labs, Impax Laboratories, Upsher-Smith Laboratories and King Pharmaceuticals (being acquired by Pfizer). In addition, companies pursuing different but related fields represent substantial competition. Many of these organizations competing with us have substantially greater capital resources, larger research and development staffs and facilities, longer drug development history in obtaining regulatory approvals and greater manufacturing and marketing capabilities than we do. These organizations also compete with us to attract qualified personnel and parties for acquisitions, joint ventures or other collaborations.

***Our success, competitive position and future revenue will depend in part on our ability to obtain and maintain patent protection for our products, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights and to operate without infringing the proprietary rights of third parties.***

We do not know whether any of our pending patent applications or those patent applications that we may file or license in the future will result in the issuance of any patents. Moreover, we cannot predict the degree of patent protection that will be afforded by those patent applications that do result in issuance. Although we generally seek the broadest patent protection available for our proprietary compounds, we may not be able to obtain patent protection for the actual composition of any particular compound and may be limited to protecting a new method of use for the compound or otherwise restricted in our ability to prevent others from exploiting the compound. If our patent protection for any particular compound is limited to a particular method of use or indication such that, if a third party were to obtain approval of the compound for use in another indication, we could be subject to competition arising from off-label use.

Moreover, our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated, rendered unenforceable or circumvented, any of which could limit our ability to stop

competitors from marketing related products. In addition, the rights granted under any issued patents may not provide us with competitive advantages against competitors with similar compounds or technologies. Furthermore, our competitors may independently develop similar technologies in a manner that does not infringe our patents or other intellectual property.

If a third party legally challenges our patents or other intellectual property rights that we own or license, we could lose certain of these rights. For example, third parties may challenge the validity of our U.S. or foreign patents through reexaminations, oppositions or other legal proceedings. If successful, a challenge to our patents or other intellectual property rights could deprive us of competitive advantages and permit our competitors to use our technology to develop similar products.

In addition, we do not anticipate having patent protection on droxidopa when and if it receives market approval by the FDA for NOH under the brand name Northera™. While the orphan drug designation for this compound by the FDA will provide seven years of market exclusivity, we will not be able to exclude other companies from manufacturing and/or selling this compound beyond that timeframe.

***Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.***

If a third party were to file a patent infringement suit against us, we could be forced to stop or delay research, development, manufacturing or sales of any infringing product in the country or countries covered by the patent infringed, unless we can obtain a license from the patent holder. Any necessary license may not be available on acceptable terms or at all, particularly if the third party is developing or marketing a product competitive with the infringing product. Even if we are able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property. We also may be required to pay substantial damages to the patent holder in the event of an infringement. If we have supplied infringing products to third parties for marketing or have licensed third parties to manufacture, use or market infringing products, we may be obligated to indemnify these third parties for any damages they may be required to pay to the patent holder and for any losses they may sustain themselves as a result.

***We may initiate patent litigation against third parties to protect or enforce our patent rights. Failure to protect our patents and other proprietary rights may materially harm our business, financial condition and results of operations.***

Legal or administrative proceedings may be necessary to defend against claims of infringement or to enforce our intellectual property rights. If we become involved in any such proceeding, irrespective of the outcome, we may incur substantial costs, and the efforts of our technical and management personnel may be diverted, which could materially harm our business. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that disclosure of some of our confidential information could be compelled and the information compromised. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments that, if perceived as negative by securities analysts or investors, could have a substantial adverse effect on the trading price of our common stock.

***Existing patents and proprietary rights could harm our competitive position.***

Other entities may have or obtain patents or proprietary rights that could limit our ability to manufacture, use, sell, offer for sale or import products or impair our competitive position. In addition, to the extent that a third party develops new technology that covers our products, we may be required to obtain licenses to that technology, which licenses might not be available or may not be available on commercially reasonable terms, if at all. Our failure to obtain a license to any technology that we require may materially harm our business, financial condition and results of operations.

***Changes in either patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.***

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. Therefore, enforceability or scope of our patents in the United States or in foreign countries cannot be predicted with certainty, and, as a result, any patents that we own or license may not provide sufficient protection against competitors.

Some jurisdictions have laws that permit the government to force a patentee to grant a license to a third party for commercialization of a patented product if the government concludes that the product is not sufficiently developed or not meeting the health needs of the population. Such compulsory licensing laws are very rarely invoked outside of South America and Africa. In addition, a number of countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may be limited to monetary relief and may be unable to enjoin infringement, which could materially diminish the value of the patent. Such compulsory licenses could be extended to include some of our product candidates, which may limit our potential revenue opportunities.

Because of the extensive time required for development, testing and regulatory review of a new drug, it is possible that any related patent may expire before any of our product candidates can be commercialized or remain in force for only a short period following commercialization. In either case, this would reduce any advantages of the patent.

***If we are unable to satisfy our obligations under current and future license agreements, we could lose license rights which would adversely affect our business.***

We are a party to a license agreement with Dr. M. Gopal Nair under which we license patent rights for our product candidate CH-4051 and other antifolates. Similarly, we license patent and/or certain other rights from DSP for droxidopa. We may enter into additional licenses in the future. Our existing licenses impose, and we expect future licenses will impose, various milestone payments, royalty payments and other obligations on us. If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business. If a licensor challenges our license position, our competitive position and business prospects could be harmed.

Our license agreement with Dr. Nair reserves rights to the licensor in India. Therefore, we will not commercialize our licensed antifolates in India. Our license agreement with DSP reserves rights to the licensor in Japan, Korea, China and Taiwan which preclude our commercialization of droxidopa in those markets.

***If we are unable to enforce trade secret protection and confidentiality agreements with our employees, our competitive position might be harmed.***

Our success also depends upon the skills, knowledge and experience of our scientific and technical personnel, our consultants and advisors, as well as our licensors and contractors. To help protect our proprietary know-how and our inventions for which patents are unobtainable or difficult to obtain, we rely on trade secret protection and confidentiality agreements. To this end, it is our policy to require all of our employees, consultants, advisors and contractors to enter into agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business. These agreements might not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information. If any of our trade secrets, know-how or other proprietary information is disclosed, the value of our trade secrets, know-how and other proprietary rights would be significantly impaired and our business and competitive position would suffer.

***If we infringe the rights of third parties we could be prevented from selling products, forced to pay damages and defend against litigation.***

If our products, methods, processes and other technologies infringe the proprietary rights of other parties, we could incur substantial costs and we might have to:

- obtain licenses, which might not be available on commercially reasonable terms, if at all;
- abandon an infringing drug candidate;
- redesign our products or processes to avoid infringement;
- stop using the subject matter claimed in the patents held by others;
- pay damages; or
- defend litigation or administrative proceedings, which might be costly whether we win or lose, and which could result in a substantial diversion of valuable management resources.

***We might not successfully manage our growth.***

We are a small, development stage company. Our success will depend upon the expansion of our operations and the effective management of our growth, which will place a significant strain on our management and on our administrative, operational and financial resources. As of March 1, 2011, we had 30 employees. We anticipate having to augment our operational, financial and management systems and hire and train even more qualified personnel. If we are unable to manage our growth effectively, our business would be harmed.

***We might be exposed to liability claims associated with the use of hazardous materials and chemicals.***

Our research and development activities might involve the controlled use of hazardous materials and chemicals. Although we believe that our safety procedures, and those of our partners, for using, storing, handling and disposing of these materials comply with federal, state, local and, where applicable, foreign laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages and any liability could materially adversely affect our business, financial condition and results of operations. In addition, the laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products might require us to incur substantial compliance costs that could materially adversely affect our business, financial condition and results of operations.

***We rely on key executive officers and scientific and medical advisors, and their knowledge of our business and technical expertise would be difficult to replace.***

As a small, development stage company, we are highly dependent on our executive officers, including particularly our Chief Executive Officer, Simon Pedder, Ph.D., and our principal scientific, regulatory, sales, marketing and medical officers and advisors. Dr. Pedder is the only executive officer whose employment with us is governed by an employment agreement, and the term of employment under that agreement expires in May 2012. We do not have “key person” life insurance policies for any of our officers. The loss of the technical knowledge and management and industry expertise of any of our key personnel could result in delays in product development, loss of any future customers and sales and diversion of management resources, which could adversely affect our operating results.

***If we are unable to hire additional qualified personnel, our ability to grow our business will be harmed.***

As a small, development stage company, we will need to hire additional qualified personnel with expertise in preclinical testing, clinical research and testing, government regulation, formulation and manufacturing, distribution and sales and marketing. We compete for qualified individuals with numerous pharmaceutical and

biopharmaceutical companies, universities and other research institutions. Competition for such individuals is intense, and we cannot be certain that our search for such personnel will be successful. Attracting and retaining qualified personnel is critical to our success.

***We might incur substantial liabilities and might be required to limit commercialization of our products in response to product liability lawsuits.***

The testing and marketing of medical products entail an inherent risk of product liability. If we cannot successfully defend ourselves against product liability claims, we might incur substantial liabilities or be required to limit commercialization of our products. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our products. Although we carry clinical trial insurance, we might not be able to renew such insurance at a reasonable cost, if at all, or our intended collaborators may be unable to obtain such insurance at a reasonable cost, if at all. Even if our agreements with any future collaborators entitle us to indemnification against losses, that indemnification might not be available or adequate should any claim arise.

**Risks Related to Our Securities**

***The prices at which shares of our common stock are traded will likely be volatile.***

You should expect the prices at which our common stock is traded to be highly volatile. Since the commencement of NASDAQ trading in May 2006, the price has varied from a low of \$1.09 to a high of \$8.41. The expected volatile price of our stock will make it difficult to predict the value of your investment, to sell your shares at a profit at any given time, or to plan purchases and sales in advance. A variety of other factors might also affect the market price of our common stock. These include, but are not limited to:

- publicity regarding actual or potential clinical results relating to products under development by our competitors or us;
- delays or failures in initiating, completing or analyzing preclinical or clinical trials or the unsatisfactory design or results of these trials;
- success or delays in commercialization of our product candidates;
- market acceptance of our product candidates;
- obtaining, delays in or rejection of regulatory approvals for our products or our competitor's products by U.S. or foreign regulators;
- announcements of technological innovations or new commercial products by our competitors or us;
- developments concerning proprietary rights, including patents;
- developments concerning our collaborations;
- regulatory developments in the United States and foreign countries;
- economic or other crises and other external factors;
- period-to-period fluctuations in our results of operations;
- changes in financial estimates by securities analysts; and
- sales of our common stock.

We will not be able to control many of these factors, and we believe that period-to-period comparisons of our financial results will not necessarily be indicative of our future performance.

In addition, the stock market in general, and the market for pharmaceutical companies in particular, has experienced extreme price and volume fluctuations that might have been unrelated or disproportionate to the operating performance of individual companies. These broad market and industry factors might seriously harm the market price of our common stock, regardless of our operating performance.

***We have never paid dividends and do not intend to pay cash dividends.***

We currently anticipate that no cash dividends will be paid on our common stock in the foreseeable future. While our dividend policy will be based on the operating results and capital needs of the business, it is anticipated that all earnings, if any, will be retained to finance our future operations.

***If securities analysts downgrade our stock or cease coverage of us, the price of our stock could decline.***

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. Currently, six financial analysts publish reports about us and our business. We do not control these or any other analysts. Furthermore, there are many large, well-established, publicly traded companies active in our industry and market, which may mean that it is less likely that we will receive widespread analyst coverage. If any of the analysts who cover us downgrade our stock, our stock price would likely decline rapidly. If these analysts cease coverage of our company, we could lose visibility in the market, which in turn could cause our stock price to decline.

***Substantial future sales of our common stock in the public market may depress our stock price and make it difficult for you to recover the full value of your investment in our shares of common stock.***

As of March 1, 2011, we had 61,846,919 shares of common stock outstanding. Substantially all of these shares are available for public sale, subject in some cases to volume and other limitations or delivery of a prospectus. The market price of our common stock may decline if our common stockholders sell a large number of shares of our common stock in the public market, or the market perceives that such sales may occur. In addition, we have outstanding options and warrants to purchase an aggregate of 5,669,930 and 3,243,544 shares, respectively, of our common stock. If these options or warrants are exercised and the shares issued upon exercise are sold, the market price of our securities may also decline. These factors also could impair our ability to raise needed capital by depressing the price at which we could sell our securities.

#### **ITEM 1B. UNRESOLVED STAFF COMMENTS.**

None.

#### **ITEM 2. PROPERTIES.**

We currently lease 13,979 square feet of office space in Charlotte, North Carolina. This lease, as amended in October 2010, will require monthly payments of approximately \$21,000 until six months after the anticipated March 2011 delivery of additional space by the landlord as agreed in the lease amendment. After the six month free rent period specified in the lease amendment ends on or about September 11, 2011, monthly rental expense will increase by approximately \$8,000 to approximately \$28,000 per month. Assuming a successful March 2011 delivery of the expansion space, the lease will expire in March 2016. The agreement calls for annual rent increases of 3%. A security deposit equal to two months' rent, or approximately \$38,000 is being held in escrow by the landlord. We believe that our current facilities are adequate to meet our needs until at least the second half of 2012.

#### **ITEM 3. LEGAL PROCEEDINGS.**

We are not subject to any material pending legal proceeding, nor are we aware of any threatened claims against us.

## PART II

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

Our common stock has been traded on the National Association of Securities Dealers Automatic Quotation System ("NASDAQ") under the symbol "CHTP" since May 2, 2006 and traded on the Over-the-Counter Bulletin Board under the symbol "CHTP.OB" from July 29, 2005 through May 1, 2006 and under the symbol "IVRC.OB" from August 18, 2004 through July 28, 2005. The following table sets forth the high and low prices of our common stock for the reported periods, as reported by NASDAQ. These quotations reflect inter-dealer prices, without retail mark-up, markdown, or commission and may not represent actual transactions.

	<u>High</u>	<u>Low</u>
<b>Fiscal year ended December 31, 2009</b>		
First Quarter .....	\$2.17	\$1.27
Second Quarter .....	\$5.00	\$1.45
Third Quarter .....	\$7.51	\$1.71
Fourth Quarter .....	\$3.42	\$2.00
<b>Fiscal year ended December 31, 2010</b>		
First Quarter .....	\$4.19	\$2.39
Second Quarter .....	\$4.50	\$1.94
Third Quarter .....	\$7.00	\$2.73
Fourth Quarter .....	\$8.10	\$4.59

As of March 1, 2011, the last sale price of our common stock on NASDAQ was \$4.22 per share. As of March 1, 2011, there were approximately 2,300 stockholders of record.

We have neither paid nor declared dividends on our common stock since our inception and do not plan to pay dividends in the foreseeable future. Any earnings that we may realize will be reinvested to finance our operations.

The market prices for securities of pharmaceutical companies, including ours, have historically been highly volatile, and the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. Factors, such as fluctuations in our operating results, announcements of technological innovations or new therapeutic products by us or others, clinical trial results, developments concerning agreements with collaborators, governmental regulation, developments in patent or other proprietary rights, public concern as to the safety of drugs developed by us or others, future sales of substantial amounts of common stock by existing stockholders and general market conditions, can have an adverse effect on the market price of our common stock.

## ITEM 6. SELECTED FINANCIAL DATA.

The following table sets forth financial data with respect to us as of and for the five years ended December 31, 2010 and the period from April 3, 2002 (inception) through December 31, 2010. The selected financial data below should be read in conjunction with the audited financial statements and related notes included elsewhere in this Annual Report on Form 10-K and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” included in Item 7.

	Years ended December 31,					Period from April 3, 2002 (Inception) through December 31, 2010
	2010	2009	2008	2007	2006	
	(In thousands, except share and per share data)					
<b>Statement of Operations Data:</b>						
Operating expenses:						
Research and development . . . . .	\$ 30,871	\$ 23,985	\$ 27,109	\$ 12,336	\$ 6,864	\$ 108,490
Sales and marketing . . . . .	2,476	2,289	1,561	1,294	642	8,957
General and administrative . . . . .	4,155	4,076	3,727	2,875	2,028	19,948
Total operating expenses . . . . .	<u>37,502</u>	<u>30,350</u>	<u>32,397</u>	<u>16,505</u>	<u>9,534</u>	<u>137,395</u>
Operating loss . . . . .	(37,502)	(30,350)	(32,397)	(16,505)	(9,534)	(137,395)
Interest income, net of expense . . . . .	172	188	1,701	1,423	863	4,521
Other income (expense) . . . . .	—	4,390	(4,390)	—	—	—
Net loss . . . . .	<u>\$ (37,330)</u>	<u>\$ (25,772)</u>	<u>\$ (35,086)</u>	<u>\$ (15,082)</u>	<u>\$ (8,671)</u>	<u>\$ (132,874)</u>
Net loss per basic and diluted share of common stock . . . . .	<u>\$ (0.91)</u>	<u>\$ (0.82)</u>	<u>\$ (1.17)</u>	<u>\$ (0.66)</u>	<u>\$ (0.46)</u>	
Weighted average number of basic and diluted common shares outstanding . . . . .	<u>41,184,623</u>	<u>31,549,739</u>	<u>30,027,031</u>	<u>22,936,780</u>	<u>18,780,638</u>	

	As of December 31,				
	2010	2009	2008	2007	2006
	(in thousands)				
<b>Balance Sheet Data:</b>					
Cash and cash equivalents . . . . .	\$ 47,593	\$ 22,295	\$ 21,533	\$ 34,076	\$ 3,111
Short-term investments, net . . . . .	—	11,450	10,306	28,638	12,786
Working capital . . . . .	34,970	12,671	20,260	57,910	14,080
Long-term investments, net . . . . .	—	—	11,329	—	—
Total assets . . . . .	48,374	34,349	44,130	63,163	16,171
Line of credit payable . . . . .	—	11,466	7,277	—	—
Deficit accumulated during the development stage . . . . .	(132,873)	(95,543)	(69,771)	(34,685)	(19,604)
Total stockholders’ equity . . . . .	35,188	12,852	24,548	57,967	14,137

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

*The following discussion of our financial condition and results of operations should be read in conjunction with the financial statements and the notes to those statements included elsewhere in this Annual Report on Form 10-K. This discussion contains predictions, estimates and other forward-looking statements that involve a number of risks and uncertainties, including those discussed under "Risk Factors" and elsewhere in this Annual Report on Form 10-K. These risks could cause our actual results to differ materially from those anticipated in these forward-looking statements.*

### Overview

We are a development stage pharmaceutical company that seeks to acquire, develop and commercialize innovative products for the treatment of a variety of human diseases. Our strategy is to develop technologies that address important unmet medical needs or offer improved, cost-effective alternatives to current methods of treatment. Specifically, we are developing a novel therapeutic agent for the treatment of symptomatic neurogenic orthostatic hypotension, or NOH, and falls related to NOH in Parkinson's disease, or PD, as well as other potentially norepinephrine related conditions and diseases including intradialytic hypotension, fibromyalgia, adult attention deficit hyperactivity disorder and chronic fatigue syndrome. We are also developing pharmaceuticals for multiple autoimmune disorders, including rheumatoid arthritis, psoriasis, inflammatory bowel disease and cancer.

Northera, our most advanced investigational product candidate, is an orally-active synthetic precursor of norepinephrine being developed for the treatment of symptomatic NOH. In Japan, Northera has been approved since 1989 and is marketed by Dainippon Sumitomo Pharma Co., Ltd., or DSP, for the treatment of symptomatic orthostatic hypotension, freezing of gait in PD and intradialytic hypotension, or IDH. We are currently seeking to register Northera in the United States for the treatment of symptomatic NOH and are conducting Phase III trials designed to support a supplemental new drug application, or sNDA, for the prevention of falls related to NOH in PD.

During 2007, the FDA granted orphan drug status to droxidopa for the treatment of symptomatic NOH and the EMA granted orphan medicinal product designation for the treatment of patients with Pure Autonomic Failure, or PAF, and patients with multiple system atrophy, or MSA. Droxidopa is currently in Phase III clinical trials designed to support the registration of droxidopa, under the brand name Northera™, in the United States for the treatment of symptomatic NOH.

We have previously completed two Phase III trials, Studies 301 and 302, of Northera for the treatment of symptomatic neurogenic orthostatic hypotension in patients with primary autonomic failure, a group of diseases including Parkinson's disease, multiple system atrophy and pure autonomic failure. The improvements in the symptoms of NOH, as measured by the orthostatic hypotension questionnaire composite score, or OHQ composite, associated with Northera treatment in our pivotal efficacy Study 301 are highly significant ( $p < 0.003$ ) and showed similar improvements ( $p < 0.05$ ) in a post-hoc analysis of Study 302 data. On that basis, we proposed filing our NDA in symptomatic NOH. During our pre-NDA meeting in December 2010, the FDA agreed that the proposed NDA for Northera could be submitted based on combined data from our two completed Phase III studies of Northera in NOH, Study 301 and Study 302, and their associated safety Studies 303, 304 and 305, without the need for any further efficacy studies. During the meeting, the FDA did request and we agreed to supply top-line results from a QTc study at the time of the 90-day safety update and conduct a post-marketing study to evaluate the clinical pharmacology of Northera in renally-impaired patients.

Upon review of anecdotal evidence in the adverse events reported in Study 302 suggesting that Northera treatment was associated with fewer falls, we decided to prospectively assess this benefit as a secondary efficacy parameter in Study 306, a Phase III trial initiated in 2010 prior to the completion of Study 301. Since Study 306 was originally intended to support our registration of Northera for the treatment of NOH, the primary endpoint

for Study 306 was the relative mean change in the OHQ composite between treatment and placebo arms. In February of 2011, we announced our plans to modify Study 306 following a futility determination at the planned interim analysis of the study's primary endpoint and an unblinded review of multiple, secondary outcome measures showing a 60% reduction in falls and supportive signs of therapeutic activity associated with Northera in the first 51 patients to complete Study 306. Given the highly significant outcome of Study 301, the FDA agreement that sufficient data exists to support an NDA filing without the results of Study 306 and given the outcome of the interim analysis, we now intend to modify Study 306 and use the data from this trial to form the basis for a future, supplemental claim of a reduction in falls associated with NOH in PD.

Having already enrolled 113 patients as of February 2011, we now plan to modify and separate Study 306 such that the first 51 patients evaluated in the unblinded interim analysis will be considered Part A (Study 306a) and constitute a hypothesis-generating study, and the remaining patients enrolled or to be enrolled in the study will become Part B (Study 306b) and serve as a distinct, hypothesis-confirming study. Based on the analysis of data from Study 306a, we currently expect to add approximately 100 additional patients to the 62 blinded patients already enrolled in Study 306b, repowering the study to demonstrate a 40% reduction in falls associated with NOH in PD. Based on these preliminary estimates, we anticipate data from Study 306b will likely be available by the second quarter of 2012. Collectively, we believe the results from Studies 306a and 306b should serve as the basis for a sNDA intended to expand the future labeling of Northera in the U.S. to include the prevention of falls in NOH associated with PD.

Our Phase II trial of droxidopa, alone and in combination with carbidopa, for the treatment of fibromyalgia continues. This trial began in early 2009 under approval from the United Kingdom's Medicines and Healthcare Products Regulatory Agency. On July 1, 2010, we announced completion and favorable outcome of an independent Data Monitoring Committee review of the safety and efficacy data from approximately half the patients expected to participate in the trial.

In February 2010, we announced that an investigator-led Phase II study of droxidopa, in combination with carbidopa, for the treatment of adult attention deficit hyperactivity disorder, or ADHD, had been initiated. In August 2010, we also announced that an investigator-led, open label Phase II study of droxidopa for the treatment of chronic fatigue syndrome, or CFS, had been initiated.

In March 2009, we announced positive results from a preliminary analysis of the completed double-blind, placebo controlled Phase II trial of droxidopa for the treatment of IDH. Droxidopa demonstrated benefit and an indication of dose response in multiple measures of IDH, particularly in alleviating serious adverse events and complications, such as dialysis disruption. In addition, an ongoing Phase II trial of droxidopa, alone and in combination with carbidopa, for the treatment of fibromyalgia began in early 2009, under approval from the United Kingdom's Medicines and Healthcare Products Regulatory Agency.

In addition to droxidopa, we are currently developing a portfolio of molecules for the treatment of various autoimmune/inflammatory diseases. The most advanced platform is a portfolio of metabolically-inert antifolate molecules engineered to have potent anti-inflammatory and anti-tumor activity to treat a range of immunological disorders, including two clinical stage product candidates designated as CH-1504 and CH-4051. In March 2009, we announced positive results from the completed Phase II head-to-head clinical trial of CH-1504 for the treatment of rheumatoid arthritis, designed to compare the efficacy and tolerability of CH-1504 against methotrexate, currently the leading antifolate treatment and standard of care for a broad range of abnormal cell proliferation diseases. The preliminary analysis showed comparable American College of Rheumatology efficacy criteria, or ACR20/50/70 response rates, to patients treated with daily 0.25mg, 0.50mg and 1.0mg of CH-1504 against patients treated with a standard weekly 20mg oral dose of methotrexate. In addition, the efficacy of CH-1504 was associated with improved tolerability and reduced hepatotoxicity compared with methotrexate. In April 2009, we announced positive findings from our Phase I study of CH-4051, the L-isomer of CH-1504. Data from this single and multiple ascending dose study demonstrated that CH-4051 is safe and well tolerated up to a maximally tolerated dose of 7.5mg.

Based on these findings, we initiated a double-blind, multiple-arm randomized Phase II study with a primary efficacy endpoint of the ACR hybrid score that combines a continuous scale of percentage improvement with the well-known ACR20/50/70 in September 2010.

Complementing our autoimmune/inflammatory program is a second platform consisting of a portfolio of therapeutics targeting immune-mediated inflammatory disorders and transplantation, known as our I-3D portfolio. We currently have no work underway related to this portfolio.

Since inception we have focused primarily on organizing and staffing our company, negotiating in-licensing agreements with our partners, acquiring, developing and securing our proprietary technology, participating in regulatory discussions with the FDA, the EMA and other regulatory agencies and undertaking preclinical trials and clinical trials of our product candidates. We are a development stage company and have generated no revenue since inception. We do not anticipate generating any product revenue until and unless we successfully obtain approval from the FDA or equivalent foreign regulatory bodies to begin selling our pharmaceutical candidates although we could potentially generate revenue by entering into strategic agreements including out-licensing, co-development or co-promotion of our drug candidates. Developing pharmaceutical products is a lengthy and expensive process. Even if we do not encounter unforeseen safety issues or timing or other delays during the course of developing our currently licensed product candidates, we would not anticipate receiving regulatory approval to market any such products until the first quarter of 2012, at the earliest. Assuming FDA approval of Northera for marketing in the United States, we currently anticipate launching the product and having initial sales or royalty revenue from it in the second quarter of 2012. Currently, development expenses are being funded with proceeds from equity financings completed in December 2004, February 2006, March 2007, November 2007, July 2009, March 2010, October 2010 and February 2011 and, to a lesser extent, proceeds from the exercise of warrants and options. In addition, we received additional proceeds under a controlled equity offering for sales made during September 2010. To the extent we move our products into additional clinical trials and expand our commercialization and marketing efforts for Northera, our need to finance operating costs will continue. Accordingly, our success depends not only on the safety and efficacy of our product candidates, but also on our ability to finance the development and/or commercialization of the products.

### ***Revenue and Cost of Revenue***

We have not generated any revenue from licensing, milestones or product sales through December 31, 2010. We do not expect to generate product revenue until and unless we receive approval from the FDA or other regulatory authorities to market our product candidates. However, we may decide to out license one or more of our drug product candidates and, if successful, we would anticipate revenue to be recorded from such a transaction. However, we might never be able to generate revenue. None of our existing product candidates are expected to be commercially available until, at the earliest, 2012, if at all.

### ***Research and Development***

Research and development expenses consist primarily of costs associated with determining feasibility, licensing and preclinical and clinical testing of our licensed pharmaceutical candidates, including salaries and related personnel costs, fees paid to consultants and outside service providers for drug manufacture and development, certain legal expenses and other expenses. All of our major research and development projects subject us to drug development and regulatory risks, including specifically risks of delays and cost over-runs that could be material to our financial condition and results of operations. For certain programs, we might rely on collaborative partners or our ability to enter into collaborations on favorable terms in order to advance a product candidate and pay a portion of the research and development expenses. See "Item 1A. Risk Factors." We expense our research and development costs as they are incurred. Research and development expenses, related to our

major research and development projects, for the years ended December 31, 2010, 2009 and 2008 were approximately \$30.9 million, \$24.0 million and \$27.1 million, respectively, and are detailed as follows:

(in thousands)	Years ended December 31,		
	2010	2009	2008
Antifolates .....	\$ 6,100	\$ 2,300	\$ 8,900
Droxidopa .....	24,800	21,700	18,200
I-3D .....	—	—	—
	<u>\$30,900</u>	<u>\$24,000</u>	<u>\$27,100</u>

### ***Sales and Marketing***

Selling and marketing expenses consist primarily of salaries and related expenses that support our business development activity, promotional expenses, expenses related to the branding, pricing and market analysis of our pharmaceutical compounds and certain legal expenses.

### ***General and Administrative***

General and administrative expenses focus on the support of administrative activities and consist primarily of salaries and related expenses for executive, finance and other administrative personnel, recruitment expenses for such personnel, consulting and professional fees and other corporate expenses, including general legal and accounting activities, certain taxes and other government fees and facilities-related expenses.

### ***Corporate History***

On February 11, 2005, we completed a merger with Ivory Capital Corporation, or Ivory, a publicly traded Colorado corporation, in which a wholly owned subsidiary of Ivory Capital was merged with and into Chelsea Therapeutics, Inc., or Chelsea Inc., and Chelsea Inc. became a wholly owned subsidiary of Ivory. The merger resulted in a change of control of Ivory, with the former stockholders of Chelsea Inc. owning approximately 96.75% of the resulting entity, after assuming the conversion of all outstanding options and warrants. In addition, the terms of the merger provided that the sole officer and director of Ivory would be replaced by the officers and directors of Chelsea Inc. The transaction was accounted for as a reverse acquisition with Chelsea Inc. as the acquiring party and Ivory as the acquired party, in substance, a reorganization of Chelsea Inc. Accordingly, when we refer to our business and financial information relating to periods prior to the merger, we are referring to the business and financial information of Chelsea Inc. unless the context indicates otherwise. On July 28, 2005, Ivory merged with Chelsea Therapeutics International, Ltd., or Chelsea Ltd., with Chelsea Ltd. as the surviving corporation. As a result, Chelsea Ltd. is the public reporting company and is the 100% owner of Chelsea Inc., its operating subsidiary.

When we refer to business and financial information for periods between January 1, 2005 and July 28, 2005, we are referring to the business and financial information of Ivory. Except as noted, all share numbers included herein reflect the conversion of every nine shares of Ivory Capital Corporation common stock for one share of Chelsea Ltd. common stock that occurred in connection with our Delaware reincorporation on July 28, 2005.

### **Results of Operations**

The tables below set forth, for the periods indicated, certain items in our consolidated statements of operations and other pertinent financial and operating data.

**Comparison of Years ended December 31, 2010 and 2009**

(in thousands, except percentages)	For the year ended December 31, 2010	For the year ended December 31, 2009	\$ Increase	% Change
Research and development expense . . . . .	\$30,871	\$23,985	\$ 6,886	29%
Sales and marketing expense . . . . .	2,476	2,289	187	8%
General and administrative expense . . . . .	4,155	4,076	79	2%
Interest income . . . . .	243	337	(94)	-28%
Interest expense . . . . .	(70)	(149)	79	-53%
Other income (expense) . . . . .	—	4,390	(4,390)	-100%

*Research and development expenses.* Based on the results of our meeting with the FDA in the fourth quarter of 2009, much of our efforts for Northera® (droxidopa) during 2010 were focused on implementing the approved changes to and completing Study 301 while also designing and initiating Study 306 upon the recommendation of the FDA. We incurred expenses associated with these and other NOH programs during 2010, along with costs related to our ongoing Phase II trial of droxidopa in fibromyalgia, costs related to the Phase II trial of our antifolates in rheumatoid arthritis, including licensing fees, and the costs of manufacturing, packaging and labeling appropriate clinical trial material for these trials. Other activities for droxidopa included manufacturing and formulation costs in support of the clinical efficacy and safety programs and activities related to validation of active pharmaceutical ingredient batches for potential commercialization. For 2009, we incurred significant expenses associated with our pivotal Phase III clinical and registration program for Northera in symptomatic NOH, along with costs related to our ongoing Phase II trial of droxidopa in fibromyalgia. In addition, we incurred costs related to our Phase II trial of CH-1504 and our Phase I trial of CH-4051, our antifolates. Also contributing to our expenses in both periods were compensation and related costs. As a percentage of operating expenses, research and development costs were 82% for the year ended December 31, 2010 compared with 79% for 2009.

*Droxidopa.* From inception through December 31, 2010, we had spent approximately \$73.9 million in research and development expenses on droxidopa. Assuming we do not enter into an out-license, co-development or other type of collaborative agreement with respect to this compound, we estimate that subsequent to that date we will need to incur approximately \$21 million more, primarily to complete our NDA filing, a QTc safety study and our Phase III extension program. These estimated costs do not include license payments or commercial drug product purchases made during this timeframe. Assuming FDA approval of droxidopa for marketing in the United States, we currently anticipate launching the product and having initial sales or royalty revenue from it in the second quarter of 2012. In addition to the spending requirements above, we plan to spend up to approximately \$12 million to complete Study 306 in support of a planned sNDA for falls related to NOH in PD and \$3 million in 2011 for clinical proof of concept studies in other indications unrelated to the NOH registration and commercialization program.

*Antifolates.* From inception through December 31, 2010, we had spent approximately \$32.1 million in research and development expenses on our portfolio of antifolates. We currently intend to seek a partner to assist us in the development of our antifolates after the completion of Phase II proof-of-concept studies for CH-4051 in rheumatoid arthritis, expected in 2012. We estimate that we will spend approximately \$10 million for this study in 2011. Assuming an approval for marketing, we currently estimate launch of this product and initial royalty revenue from it no sooner than 2014.

*I-3D Portfolio.* From inception through December 31, 2010, we had spent approximately \$2.5 million in research and development expenses on the I-3D portfolio of compounds. We have conducted compound discovery work on the portfolio to try and identify one or more lead compounds. All of the work completed to date was performed before 2008 and we do not expect to incur significant additional expenses for these compounds until we select a partner or obtain additional financing.

*Sales and marketing expenses.* Although we had no formalized selling activities, in 2010 we incurred increases in sales and marketing expenses for compensation and related expenses and promotional costs that include conference sponsorships offset by decreases in legal expenses related to our intellectual property and market research costs. During 2009, we incurred expenses of a similar nature, with more market research activity and less promotional activity than in 2010. We anticipate a significant increase in sales and marketing spending in 2011 as we prepare for the commercialization of Northera in the United States. We currently expect such spending will be between \$10 and \$14 million.

*General and administrative expenses.* During 2010, we incurred small increases in compensation and related costs, computer and software expenses and insurance expenses, offset by decreases in professional fees for legal and accounting services and travel expenses.

*Interest income and interest expense.* At December 31, 2010, we had cash and cash equivalents of \$47.6 million. We received interest income on auction rate securities, or ARS, during the first six months of 2010 for ARS that were redeemed on June 30, 2010 and during 2009 for ARS that were redeemed in the second quarter of 2009 as well as those redeemed in 2010. The decrease reflects the loss of the premium interest rates for those investments. Interest expense decreased as the line of credit associated with our investments in ARS held at UBS was fully paid on June 30, 2010.

*Other (income) expense.* During the year ended December 31, 2009, we recorded a gain of \$4.4 million on the recovery of previously recorded impairment losses for ARS that were redeemed at par and an increase in the fair value of our ARS Rights.

#### **Comparison of Years ended December 31, 2009 and 2008**

(in thousands, except percentages)	For the year ended December 31, 2009	For the year ended December 31, 2008	\$ Increase (Decrease)	% Change
Research and development expense . . . . .	\$23,985	\$27,109	\$(3,124)	-12%
Sales and marketing expense . . . . .	2,289	1,561	728	47%
General and administrative expense . . . . .	4,076	3,727	349	9%
Interest income . . . . .	337	1,707	(1,370)	-80%
Other income (expense) . . . . .	4,390	(4,390)	8,780	n/a

*Research and development expenses.* We continued to incur significant development expenses in 2009, primarily related to our extensive clinical testing programs, particularly, clinical activities for droxidopa, including our pivotal Phase III trials in NOH and Phase II trial in fibromyalgia. In addition, we incurred costs associated with our Phase II study of CH-1504 in rheumatoid arthritis, completed in March 2009, and our Phase I dosing study of CH-4051, completed in April 2009. Other activities contributing to expenses in 2009 include manufacture, formulation, labeling and packaging and regulatory costs. As a percentage of operating expenses, research and development costs were 79% for the year ended December 31, 2009 compared with 84% for the same period of 2008. Also contributing to our expenses were compensation and related costs in both periods. A significant component of our costs in 2008 was related to the ongoing Phase II clinical trial for CH-1504 in rheumatoid arthritis and investigational activities for follow-on molecules in our portfolio of antifolates. We also incurred significant costs during 2008 for clinical activities for droxidopa including the start of our Phase III programs in NOH and our Phase II study in IDH. Other activities for droxidopa included manufacturing and formulation costs in support of the clinical programs and license milestone payments for dosing in a Phase III trial.

*Sales and marketing expenses.* Although we had no formalized selling activities, the increase in sales and marketing expenses in 2009 were attributable to costs of initiating market research and commercialization activities for droxidopa in anticipation of positive results of Study 302. In addition, we performed market

analysis studies for both droxidopa and our antifolates. Other expenses included compensation and related costs, legal expenses and related costs for our intellectual property and travel costs for our business development efforts. During 2008, we incurred expenses of a similar nature but rather than preliminary marketing activities related to the planned commercialization of droxidopa, our efforts were focused on the printing of educational materials and a pricing study for droxidopa.

*General and administrative expenses.* The increase in general and administrative expenses primarily consists of an increase in compensation and related expenses. The remainder of the increase is related to moderate increases in other categories of spending during the period including office rent related to our headquarters and professional fees for accounting services offset by a decrease in franchise tax expense due to the impact of 2008 operating losses on the taxable equity base.

*Interest income.* At December 31, 2009, we had cash and cash equivalents of \$22.3 million and short-term investments of \$11.45 million. Although the funding received from our July 2009 financing, proceeds from the sale and redemption of ARS and additional funding under the line of credit we have with UBS allowed us to maintain a higher than expected average cash and investments level over the period, the average cash and investment level during 2009 was significantly lower than the level for the same period of 2008. When those lower average levels are combined with the loss of interest income on ARS earned in 2008, the deterioration of overall market interest rates and a shift of our holdings in 2008 and 2009, other than ARS, into non-interest bearing accounts, Treasury funds, low-yielding commercial money market account and similar investments, interest earned decreased by \$1.4 million.

*Other (income) expense.* During the year ended December 31, 2009, we recorded a gain of \$4.4 million on the recovery of previously recorded impairment losses for ARS that were redeemed at par and an increase in the fair value of our ARS Rights. During the year ended December 31, 2008, we had recorded the subsequently recovered other-than-temporary impairment loss related to our investments in ARS of approximately \$4.4 million.

## **Liquidity and Capital Resources**

From inception to December 31, 2010, we have incurred an aggregate net loss of approximately \$132.9 million as a result of expenses similar in nature to those described above.

As of December 31, 2010, we had working capital of approximately \$35 million and cash and cash equivalents of approximately \$47.6 million. We have financed our operations primarily through sales of our stock and, to a much lesser extent, through the issuance of our common stock pursuant to option or warrant exercises. Cash on hand results primarily from previous financing activities offset by funds utilized for operating and investing activities. Our financing activities are more fully described in “Financings” below.

During 2010, we successfully redeemed, at full par value, all of our holdings in ARS. At December 31, 2009, we held short-term investments of \$11.45 million, consisting of principal invested in certain ARS and the fair value of the ARS Rights. Our investments in these securities represented interests in collateralized debt obligations supported by pools of structured credit instruments consisting of student loans. None of the collateral for the ARS held by us included mortgage, credit card or insurance securitizations. During the year ended December 31, 2010, approximately \$5.3 million of our investments in ARS were redeemed at full par value. On June 30, 2010, we exercised our right, as outlined under the settlement agreement with UBS, to sell the remaining ARS investments of approximately \$6.2 million, along with our ARS rights, to UBS at par value.

During the fourth quarter of 2008, we accepted the terms of the settlement agreement from UBS for ARS Rights for our illiquid ARS holdings purchased from and maintained at UBS as of February 13, 2008. The ARS Rights provided us with the ability to sell the ARS, along with the ARS Rights, to UBS at the par value of the ARS no earlier than June 30, 2010 and expired on July 2, 2012. UBS also agreed that an affiliate would provide

us with a no net-cost line of credit for up to a portion of the market value (as determined by UBS) of our ARS holdings as of October 31, 2008. In March 2009, the line of credit was amended to provide us with a credit line of up to the full par value of our ARS holdings at UBS and, accordingly, we had fully drawn down the line of credit and had recorded a corresponding liability at December 31, 2009 of \$11.47 million, including accrued interest. We repaid the line of credit with the proceeds from redemptions during the year ended December 31, 2010 and offset the remaining balance at June 30, 2010 with the exercise of our ARS Rights on June 30, 2010.

Per the terms of a settlement agreement executed in May 2009, all of our ARS holdings that were then classified as available-for-sale and had been purchased from Banc of America Securities, or BA, were redeemed at 100% of par value, or \$11.6 million, in June 2009. In addition, BA also refunded to us the \$0.4 million realized loss we incurred in January 2009 upon the sale of our \$2.5 million par value ARS holding in Mississippi Higher Ed Assistance Corp. As such, we recorded a gain of approximately \$4.1 million related to the recovery of the previously recorded other-than-temporary impairment for these ARS holdings.

### **General**

We have incurred negative cash flows from operations since inception. We have spent, and expect to continue to spend, substantial amounts in connection with implementing our business strategy, including our planned product development efforts, our clinical trials, our commercialization and marketing activities for droxidopa and our efforts to secure opportunities for strategic alliances.

Our continued operations depend on our ability to raise funds through various potential sources, such as equity and debt financing, the exercise of warrants or strategic alliances. Such strategic relationships or out-licensing arrangements might require us to relinquish rights to certain of our technologies, product candidates or products that we would otherwise seek to develop or commercialize ourselves. Such additional funds might not become available on acceptable terms, or at all, and there can be no assurance that any additional funding that we do obtain will be sufficient to meet our needs.

We believe that our capital resources available at December 31, 2010, when combined with proceeds of approximately \$8.4 million from the exercise of warrants that expired in February 2011 and net proceeds of \$37.8 million from our equity offering completed in February 2011 will be sufficient to meet our operating needs into the second quarter of 2012, including an increasing level of commercialization activity and expenses related to the anticipated market launch of Northera in the United States which we expect no sooner than the second quarter of 2012.

Strategic relationships or out-licensing arrangements might require us to relinquish rights to certain of our technologies, product candidates or products that we would otherwise seek to develop or commercialize ourselves. Such additional funds might not become available on acceptable terms, or at all, and there can be no assurance that any additional funding that we do obtain will be sufficient to meet our needs.

From inception through December 31, 2010 we had losses of \$132.9 million. We had net losses of \$37.3 million, \$25.8 million and \$35.1 million for the years ended December 31, 2010, 2009 and 2008, respectively, and we anticipate losses at least through 2011 unless we should successfully negotiate a strategic agreement earlier that might include out-licensing, co-development or co-promotion of one or more of our drug candidates. Actual losses will depend on a number of considerations including:

- continuing discussions with regulatory agencies concerning the design and results of our clinical trials;
- the pace and success of development activities, including programs for droxidopa, antifolates and other product candidates;
- our ability to identify and recruit patients into our clinical trials at costs consistent with our current estimates;
- seeking regulatory approval for our various product candidates;

- the pace of commercialization and marketing efforts for Northera;
- possible out-licensing of our product candidates;
- the pace of development of new intellectual property for our existing product candidates;
- in-licensing and development of additional product candidates;
- implementing additional internal systems and infrastructure; and
- hiring additional personnel.

Should we raise additional funds by selling shares of common stock or other securities convertible into common stock, the ownership interest of our existing stockholders will be diluted. If we are not able to obtain financing when needed, we may be required to delay, reduce the scope of, or eliminate one or more of our development programs or curtail operations. As a result, our business, financial condition and results of operations would be materially harmed.

### ***Financings***

#### 2011 Shelf Registration Statement

In February 2011, we raised gross proceeds of approximately \$40.3 million through the sale of 10,062,500 shares of our common stock in a publicly-marketed offering. These shares were offered pursuant to our shelf registration statement as filed with the Securities and Exchange Commission, or SEC, under which we may offer shares of common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of \$60,000,000. Such registration statement became effective as of January 19, 2011. In connection with this offering, we paid commissions and other offering-related costs of approximately \$2.5 million, resulting in net proceeds of approximately \$37.8 million.

#### 2009 Shelf Registration Statement

In October 2010, we raised gross proceeds of approximately \$40.3 million through the sale of approximately 8.2 million shares of common stock in a publicly-marketed offering pursuant to our shelf registration statement, as amended pursuant to Rule 462(b), as filed with the SEC under which we could offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of \$61,566,686. Such registration statement became effective as of August 20, 2009. In connection with this offering, we paid commissions and other offering-related costs of approximately \$2.5 million.

In July 2010, we filed the required documents and became eligible to use an at-the-market common equity sales program for the sale of up to 3,000,000 shares of common stock pursuant to our 2009 shelf registration statement. In September 2010, we sold 634,500 shares of common stock under this program resulting in net proceeds, after expenses for the program, of approximately \$2.9 million.

On March 5, 2010, we raised gross proceeds of approximately \$18.2 million through the sale of 6,700,000 shares of common stock plus warrants for the purchase of 2,345,000 shares of common stock. These warrants had an aggregate fair value of approximately \$3.9 million, permit the holders to purchase the underlying common shares at \$2.79 each or elect a net share settlement and are exercisable in whole at any time, or in part from time to time, during the period commencing six months after the date of issuance and ending three years from the date of issuance. These shares were offered pursuant to our 2009 shelf registration statement. In connection with this offering, we paid commissions and other offering-related costs of approximately \$1.5 million.

There are no more securities available under the 2009 shelf registration statement.

## 2007 Shelf Registration Statement

On July 28, 2009, we raised gross proceeds of approximately \$13.3 million through the sale of 3,325,000 shares of common stock. These shares were offered pursuant to our shelf registration statement filed with the SEC that became effective October 11, 2007, as amended pursuant to Rule 462(b), effective July 22, 2009, to increase the dollar amount of securities available for sale, as filed with the SEC under which we could offer shares of common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of \$62,218,060. In connection with the July 2009 offering, we received net proceeds, after deducting placement fees and offering expenses, of approximately \$12.4 million.

On November 8, 2007, we raised gross proceeds of approximately \$48.9 million through the sale of 7,388,172 shares of our common stock in a registered direct offering. These shares were offered pursuant to our 2007 shelf registration statement as filed with the SEC, under which we were able to offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of \$60.0 million, prior to its amendment. Such registration statement became effective as of October 11, 2007. In connection with this offering, we paid commissions and other offering-related costs of approximately \$3.2 million.

There are no more securities available under the 2007 shelf registration statement.

## Private Placements

On March 22, 2007, we raised gross proceeds of approximately \$12.5 million through the private placement of 2,648,306 shares of our common stock plus warrants for the purchase of 794,492 shares of our common stock. The aggregate fair value of these warrants was approximately \$1.3 million. The warrants permit the holders to purchase the underlying common shares at \$5.66 each and are exercisable in whole at any time, or in part from time to time, for cash, for five years from the date of issuance. The warrants are redeemable at par value at our option in the event that the volume weighted-average closing price of our common stock is greater than \$12.00 per share for any 20 consecutive trading days provided we give 60 business days' written notice to the holders and simultaneously call all warrants on the same terms. Under the terms of the placement agreement, we agreed to and filed a registration statement with the SEC within 30 days of the closing for the shares of common stock sold and the shares of common stock underlying the warrants and such registration became effective on August 7, 2007. In connection with this offering, we paid commissions and other offering-related costs of approximately \$1.0 million in cash.

On February 13, 2006, we raised gross proceeds of approximately \$21.5 million through the private placement of 7,166,666 shares of our common stock plus warrants for the purchase of 2,149,999 shares of our common stock. The aggregate fair value of these warrants was approximately \$1.1 million. The warrants permitted the holders to purchase the underlying common shares at \$4.20 each and were exercisable in whole at any time, or in part from time to time, for cash, for five years from the date of issuance. In addition, these warrants were redeemable at our option in the event that the volume weighted average closing bid price of our common stock for any 20 consecutive trading days is at least \$9.00 per share. In connection with this offering, we paid commissions and other offering-related costs of approximately \$1.6 million in cash and issued warrants to the placement agent for the purchase of 716,666 shares of our common stock with an exercise price of \$3.30 per share, or 110% of the price of the shares sold in the offering and an aggregate fair value of approximately \$0.7 million. These warrants are exercisable in whole at any time, or in part from time to time, for cash or in a net share settlement, for seven years from the date of issuance. Under the terms of the financing, we filed a registration statement with the SEC within 30 days of the closing for the shares of common stock sold and the shares of common stock underlying the warrants and such registration became effective on March 29, 2006.

In December 2004, we raised gross proceeds of approximately \$14.5 million through the private placement of 5,532,994 shares of our common stock. The amount raised included the conversion of a \$1.7 million stockholder loan along with accrued interest, for which a total of 677,919 shares of common stock were issued. In connection with this offering, we paid commissions and other offering-related costs of approximately \$1.0

million in cash and issued warrants to the placement agent for the purchase of 483,701 shares of our common stock with an aggregate fair value of approximately \$14,000. The warrants permit the holders to purchase the underlying common shares at \$2.88 per share, and are exercisable in whole at any time, or in part from time to time, for cash or in a net share settlement, for seven years from the date of issuance.

### ***License Agreement and Development Agreement Obligations***

In March 2004, we entered into a License Agreement with Dr. M. Gopal Nair, Ph.D., of the University of South Alabama College of Medicine, for rights to use, produce, distribute and market products derived from an invention by Dr. Nair, claimed in US Patent # 5,912,251, entitled “metabolically inert anti-inflammatory and antitumor antifolates”, designated by us as CH-1504 and related compounds. The license provides us exclusive, worldwide (excluding India) rights for these compounds.

In 2004, as consideration for these rights, we paid \$150,000 and issued Dr. Nair and his designees 471,816 shares of common stock at an estimated aggregate value of \$402. As additional consideration, we agreed to pay to Dr. Nair and or his designees: (1) royalties on the sales should any compounds be approved for commercial sale; (2) milestone payments, payable upon achievement of clinical milestones; and (3) payments to be made on specified anniversary dates, some of which were payable in equity, at our discretion. There are no minimum royalties under the agreement. We made milestone payments as required by the agreement of \$100,000 each in March 2006 and 2005. In April 2007, we issued 26,643 shares of our common stock, subject to trading restrictions, at a value of approximately \$5.63 per share, in settlement of the \$150,000 annual milestone payment for 2007. In March 2008, we made a milestone payment of \$100,000 related to patient dosing in a Phase II study as required by the agreement. In April 2008, we issued 30,612 shares of common stock, subject to trading restrictions, at a value of approximately \$4.90 per share, in settlement of the 2008 anniversary milestone payment of \$150,000. In April 2009, we made the 2009 anniversary milestone payment of \$150,000. We are also obligated to make future potential milestone payments based on the achievement of specific development and regulatory approval milestones. Based on our current development plans for compounds licensed under this agreement, approximately \$1.5 million of payments may become due if specific milestones are achieved, subject to our right to terminate the license agreement. In addition, should we enter into an out-licensing agreement, such payments could be offset by revenue received from the sub-licensee.

The license agreement includes certain other covenants, which require us to, among other things, maintain and prosecute patents related to the license; use commercially reasonable best efforts to bring the licensed product to market as soon as reasonably practicable and continue active, diligent marketing efforts; and prepare and provide to the licensors certain reports concerning our development and commercialization efforts. In the event we fail to carry out our responsibilities under the license agreement, the licensors may terminate the license. We may elect to abandon the maintenance and prosecution of any patent applications or issued patents and we retain the right to terminate the license agreement in whole or as to any portion by providing written notice of such intentions to the licensor. The license agreement may also be terminated in the event we fail to make a scheduled milestone or royalty payment, we otherwise materially breach the license agreement, or if we become involved in a bankruptcy, insolvency or similar proceeding, provided that we are entitled to notice of such intention to terminate and an opportunity to cure. Regardless, the license agreement shall expire concurrent with the date of the last to expire claim contained in the patent rights.

In May 2006, we entered into an agreement with Dainippon Sumitomo Pharma Co., Ltd., or DSP, for a worldwide, exclusive, sub-licensable license and rights to certain intellectual property and proprietary information relating to droxidopa including, but not limited to all information, formulations, materials, data, drawings, sketches, designs, testing and test results, records and regulatory documentation. As consideration for these rights, we paid DSP \$100,000 and issued 63,131 shares of our common stock, with a value of approximately \$4.35 per share, or \$274,621. As additional consideration, we agreed to pay DSP and or its designees: (1) royalties on the sales should any compound be approved for commercial sale; and (2) milestone payments, payable upon achievement of milestones as defined in the agreement. In January 2007, we received notification that the FDA had granted orphan drug designation for droxidopa for the treatment of symptomatic neurogenic orthostatic hypotension. Based on the terms of the DSP agreement, the granting of orphan drug

designation for droxidopa triggered a milestone payment to DSP of \$250,000. We made such payment in February 2007. In February 2008, we made a milestone payment under the agreement of \$500,000 related to patient dosing in a Phase III study. At December 31, 2010, remaining potential future milestone payments, subject to our right to terminate the license agreement, totaled \$3.25 million.

Subsequent to execution of the agreement, we agreed that DSP would initiate, and we would fund, activities focused on modifying the manufacturing capabilities of DSP in order to expand capacity and comply with cGMP regulations and all existing manufacturing requirements of the FDA. Based on work performed by DSP as of December 31, 2010, we had recorded expense of approximately \$3.3 million and had a remaining liability of \$0.4 million at December 31, 2010.

In May 2006, we entered into a development and commercialization agreement with Active Biotech AB to co-develop and commercialize the I-3D portfolio of orally active, dihydroorotate dehydrogenase (DHODH) inhibiting compounds for the treatment of autoimmune diseases and transplant rejection. Under the terms of the development agreement, an initial payment of \$1.0 million was made to Active Biotech during 2006 with such funds utilized to cover the initial costs of research and development efforts jointly approved by both parties. At December 31, 2006, we had expensed the entire \$1.0 million payment. At December 31, 2007, we had expensed cumulative costs of \$1.0 million under the program, in excess of the initial payment of \$1.0 million, related to costs of research and development. During 2008, we ceased joint discovery efforts with Active Biotech on this portfolio and, accordingly, recorded no costs related to this program during 2010, 2009 or 2008. In April 2008, we entered into a termination and assignment agreement with Active Biotech, whereby Active Biotech discontinued its participation in the I-3D co-development program and assigned its entire right, title and interest in the portfolio to us in exchange for royalties on future sales. The termination agreement also eliminated our obligation related to payment of potential future development milestones under the development agreement.

### ***Current and Future Financing Needs***

We have incurred negative cash flow from operations since inception. We have spent, and expect to continue to spend, substantial amounts in connection with implementing our business strategy, including our planned product development efforts, our clinical trials, our research and discovery efforts and our marketing and branding initiatives. Based on capital resources available at December 31, 2010, combined with proceeds of approximately \$8.4 million from the exercise of warrants expiring in February 2011 and proceeds of approximately \$37.8 million from the stock offering completed in February 2011, we believe that we have sufficient capital resources to meet our operating needs into the second quarter of 2012, including an increasing level of commercialization activity and expenses related to the anticipated market launch of Northera in the United States which we expect no sooner than the second quarter of 2012.

Potential sources of additional liquidity include strategic relationships, out-licensing of our products, public or private sales of equity or debt, the exercise of warrants by our warrant holders and other sources. We might seek to access the public or private equity markets again when and if conditions are favorable due to our long-term capital requirements. It is uncertain whether additional funding will be available when we need it on terms that will be acceptable to us, or at all. If we raise funds by selling additional shares of common stock or other securities convertible into common stock, the ownership interest of our existing stockholders will be diluted. If we are not able to obtain financing when needed, we might be unable to carry out our business plan. As a result, we might have to significantly delay certain activities or limit our operations and our business, financial condition and results of operations would be materially harmed.

### **Off-Balance Sheet Arrangements**

We do not have any unconsolidated entities, and accordingly, we have not entered into any transactions with unconsolidated entities whereby we have financial guarantees, subordinated retained interests, derivative instruments or other contingent arrangements that expose us to material continuing risks, contingent liabilities, or any other obligations under a variable interest in an unconsolidated entity that provides us with financing, liquidity, market risk or credit risk support.

## Contractual Obligations and Commitments

As of December 31, 2010, we have known contractual obligations and commitments of approximately \$23.3 million, primarily related to contracted research and development activities. To facilitate an understanding of our contractual obligations and commercial commitments, the following data is provided as of December 31, 2010:

Category	Payments due by period				
	Total	< 1 Year	1-3 Years	3-5 Years	More than 5 Years
Operating lease obligations . . . . .	\$ 1,866,445	\$ 290,274	\$ 740,656	\$769,753	\$65,762
Purchase obligations . . . . .	21,479,246	20,393,221	1,086,025	—	—
Total . . . . .	<u>\$23,345,691</u>	<u>\$20,683,495</u>	<u>\$1,826,681</u>	<u>\$769,753</u>	<u>\$65,762</u>

In addition, we have entered into certain other agreements that, based on our development and commercialization plans as of December 31, 2010, might require us to make contingent milestone payments of up to approximately \$4.75 million over the life of the agreements upon the achievement of certain clinical or commercial milestones. Such future payments are subject to our right to terminate the agreements. In the event that the milestones are not achieved, we elect not to pursue further testing of the drug candidate or we terminate such agreements, we will have no further obligations under the agreements. The uncertainty relating to the timing and occurrence of the commitments described prevents us from including them in the table above.

## Critical Accounting Policies

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States of America. Our significant accounting policies are more fully described in Note 1 to the consolidated financial statements accompanying this Annual Report on Form 10-K. The following accounting policies are critical in fully understanding and evaluating our reported financial results.

### *Use of Estimates*

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent liabilities at the date of the financial statements as well as the reported revenue and expenses during the reporting periods. On an ongoing basis, management evaluates its estimates and judgments. Management bases estimates on historical experience and on various other factors that it believes are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results might differ from these estimates under different assumptions or conditions.

### *Research and Development*

Research and development expenditures are expensed as incurred. We often contract with third parties to facilitate, coordinate and perform agreed upon research and development activities. To ensure that research and development costs are expensed as incurred, we measure expense based on work performed for the underlying contract, typically utilizing a percentage-of-completion approach, and record prepaid assets or accrue expenses on a monthly basis for such activities based on the measurement of liability from expense recognition and the receipt of invoices.

These contracts typically call for the payment of fees for services at the initiation of the contract and/or upon the achievement of certain milestones. In the event that we prepay fees for future milestones, we record the prepayment as a prepaid asset and amortize the asset into research and development expense over the period of time the contracted research and development services are performed. Most fees are incurred throughout the contract period and are expensed based on their percentage of completion at a particular date.

These contracts generally include pass through fees. Pass through fees include, but are not limited to, regulatory expenses, investigator fees, travel costs, and other miscellaneous costs including shipping and printing fees. Because these fees are incurred at various times during the contract term and they are used throughout the contract term, we record a monthly expense allocation to recognize the fees during the contract period. Fees incurred to set up the clinical trial are expensed during the setup period.

We have contracted with a third-party to manufacture commercial quantities of Northera prior to the date we anticipate that Northera will receive final regulatory marketing approval and might perform similar activities with other product candidates in the future. The scale-up and commercial production of pre-launch inventories involves the risk that such products may not be approved for marketing by the appropriate regulatory agencies on a timely basis, or ever. As such, until final approval to market any our product candidates is received from the appropriate regulatory agencies, such costs are expensed to research and development.

Costs related to the acquisition of technology rights and patents for which development work is still in process are expensed as incurred and considered a component of research and development costs.

### ***Accounting for Stock-Based Compensation***

We account for our stock options utilizing the fair value based method of accounting for stock options or similar equity instruments. In determining the fair value of the equity instrument, we consider, among other factors, (i) the risk-free interest rate, (ii) the expected life of the options granted, (iii) the anticipated dividend yield, (iv) the estimated future volatility of the underlying shares and (v) anticipated future forfeitures. To determine the risk-free interest rate, we utilize the U.S. Treasury yield curve in effect at the time of grant with a term consistent with the expected life of our awards. We estimate the expected life of the options granted based on anticipated exercises in future periods assuming the success of our business model as currently forecasted. The expected dividends reflect our current and expected future policy for dividends on our common stock. To determine the expected stock price volatility for our stock options, we examine historical volatilities for industry peers closely related to the current status of our business, but with sufficient trading history to be able to determine volatility. Utilizing a weighted average calculation to account for the limited price history of our stock, we analyze the historical volatility of our stock price in combination with the historical volatility of the industry peers selected to determine an appropriate volatility factor. During the fourth quarter of 2010, we began to rely solely on the historical volatility of our stock price as we had sufficient historical data for our common stock upon which to base our calculation. Given the limited service period for our current employees and the senior nature of the roles for those employees, we had estimated that we would experience no forfeitures or that our rate of forfeiture would be immaterial to the recognition of compensation expense for those options currently outstanding. Our results of operations include non-cash compensation expense as a result of the issuance of stock option grants utilizing this method. We expect to record additional non-cash compensation expense in the future, which might be significant. Due to the limited amount of historical data available to us, particularly with respect to stock-price volatility, employee exercise patterns and forfeitures, actual results could differ from our assumptions.

### **ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.**

We invest our cash in a variety of financial instruments in order to preserve principal and liquidity while maximizing returns and we do not invest in financial instruments or their derivatives for trading or speculative purposes. To minimize the exposure due to adverse shifts in interest rates, we maintain investments of shorter maturities. Our investment guidelines include security type, credit quality and maturity and are intended to limit market risk by restricting our investments to high quality debt instruments with relatively short maturities. During 2010, a portion of our cash was maintained in non-interest bearing accounts at federally insured financial institutions that, under the Temporary Liquidity Guarantee Program, were fully insured by the Federal Deposit Insurance Corporation, or FDIC, until December 31, 2010. Such accounts will be covered through December 31, 2012 under the FDIC's Transaction Account Guarantee program. In addition, we maintained and continue to

maintain funds on deposit in commercial accounts that include non-interest bearing commercial checking accounts, fully liquid interest-bearing money market accounts, certificates of deposit and Treasury funds with a maturity under 90 days. All deposits and investments to date have been made in U. S. dollars and, accordingly, have no exposure to foreign currency rate fluctuations.

Our interest income is sensitive to changes in the general level of interest rates in the United States, particularly since our investments are and will be in short-term investments. Currently, the returns on such short-term, fully liquid cash investments are at historic lows. Accordingly, we estimate that any sensitivity experienced due to fluctuations of interest rates in the United States for such investments would have no material impact on our consolidated financial position or results of operations.

## ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA.

(a) The financial statements required to be filed pursuant to this Item 8 are appended to this Annual Report on Form 10-K. An index of the financial statements filed herewith is found on page 58.

(b) The unaudited quarterly financial data for the two-year period ended December 31, 2010 is as follows:

	Year ended December 31, 2009			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Operating expenses	\$ 7,854,679	\$ 9,411,369	\$ 7,085,736	\$ 5,998,448
Loss from operations	(7,854,679)	(9,411,369)	(7,085,736)	(5,998,448)
Other income (expense)	426,412	4,127,997	(8,117)	32,026
Net loss	(7,428,267)	(5,283,372)	(7,093,853)	(5,966,422)
Basic and diluted net loss per share (a)	(0.25)	(0.18)	(0.22)	(0.18)

	Year ended December 31, 2010			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Operating expenses	\$ 6,266,607	\$ 9,990,867	\$ 8,803,675	\$ 12,441,414
Loss from operations	(6,266,607)	(9,990,867)	(8,803,675)	(12,441,414)
Other income (expense)	34,598	66,542	16,948	54,405
Net loss	(6,232,009)	(9,924,325)	(8,786,727)	(12,387,009)
Basic and diluted net loss per share (a)	(0.18)	(0.25)	(0.22)	(0.25)

(a) Basic and diluted net loss per share for each of the quarters presented above is based on the respective weighted average number of common shares for the quarters. As such, the sum of the quarters may not necessarily be equal to the full year loss per share amount. Basic and diluted net loss per share are identical since potentially dilutive securities are excluded from the calculations, as the effect would be anti-dilutive for all periods presented.

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

None.

## ITEM 9A. CONTROLS AND PROCEDURES.

### Disclosure Controls and Procedures

Disclosure controls and procedures as defined in Rule 13a-15(e) under the Securities Exchange Act of 1934, or the Exchange Act, are designed only to provide reasonable assurance that they will meet their objectives that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and

reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosures. As of the end of the period covered by this report, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rule 13a-15(e)) pursuant to Exchange Act Rule 13a-15. Based upon that evaluation and subject to the foregoing, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures were effective as of December 31, 2010.

#### **Changes in internal control over financial reporting.**

Management has determined that, as of December 31, 2010, there were no changes in our internal control over financial reporting that occurred during our fiscal quarter then ended that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

#### **Management's Report on Internal Control Over Financial Reporting**

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States. However, all internal control systems, no matter how well designed, have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and reporting.

Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2010. In making this assessment, management used the criteria set forth by the Committee of the Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework and the Guidance for Smaller Public Companies as published by COSO in June 2006. Based on that assessment, management believes that we maintained effective internal control over financial reporting as of December 31, 2010, based on those criteria.

Ernst & Young LLP, our independent registered public accounting firm, which has audited the financial statements included in Part IV, Item 15 of this report, has also audited our internal control over financial reporting as of December 31, 2010, as stated in their report, which is included below.

## **Report of Independent Registered Public Accounting Firm on Internal Control over Financial Reporting**

The Board of Directors and Stockholders  
Chelsea Therapeutics International, Ltd. and Subsidiary

We have audited Chelsea Therapeutics International, Ltd and Subsidiary'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). Chelsea Therapeutics International, Ltd. and Subsidiary'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, Chelsea Therapeutics International, Ltd. and Subsidiary 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 of Chelsea Therapeutics International, Ltd. and Subsidiary (a development stage company) as of December 31, 2010 and 2009, and the related consolidated statements of operations, changes in stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2010, and for the period from April 3, 2002 (inception) through December 31, 2010 of Chelsea Therapeutics International, Ltd. and Subsidiary and our report dated March 2, 2011 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Raleigh, North Carolina  
March 2, 2011

### **ITEM 9B. OTHER INFORMATION.**

Not applicable.

### **PART III**

#### **ITEM 10. DIRECTORS AND EXECUTIVE OFFICERS OF THE REGISTRANT.**

Incorporated by reference from the information under the headings “Proposal One – Election of Directors” and “Section 16(a) Beneficial Ownership Reporting Compliance” in our proxy statement for the 2011 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this report relates.

The information required by Item 10 with respect to identification of our executive officers has been included in Item 1 of this Form 10-K in reliance on General Instruction G of Form 10-K and Instruction 3 to Item 401(b) of Regulation S-K.

#### **ITEM 11. EXECUTIVE COMPENSATION.**

Incorporated by reference from the information under the headings “Director Compensation for Fiscal Year 2010” and “Executive Compensation and Other Matters” in our proxy statement for the 2011 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this report relates.

#### **ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS.**

Incorporated by reference from the information under the headings “Security Ownership of Certain Beneficial Owners and Management” and “Equity Compensation Plan Information” in our proxy statement for the 2011 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this report relates.

#### **ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE.**

Incorporated by reference from the information under the headings “Certain Transactions with Related Persons”, “Proposal One – Election of Directors” and “Corporate Governance Matters” in our proxy statement for the 2011 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this report relates.

#### **ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES**

Incorporated by reference from the information under the heading “Audit Committee Report” in our proxy statement for the 2011 Annual Meeting of Stockholders, which we will file with the SEC within 120 days of the end of the fiscal year to which this report relates.

**PART IV**

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

(a) Financial Statements.

The following statements are filed as part of this report:

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Reports of Independent Registered Public Accounting Firms .....	F-1
Consolidated Balance Sheets .....	F-3
Consolidated Statements of Operations .....	F-4
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Notes to Consolidated Financial Statements. ....	F-11

Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

## (b) Exhibits.

<u>Exhibit Number</u>	<u>Description of Document</u>	<u>Registrant's Form</u>	<u>Dated</u>	<u>Exhibit Number</u>	<u>Filed Herewith</u>
1.1	Placement Agency Agreement dated November 1, 2007 by and among Chelsea Therapeutics International, Ltd., Leerink Swann LLC, Oppenheimer & Co. Inc. and Punk Ziegel & Company.	8-K	11/02/07	1.1	
1.2	Placement Agency Agreement dated July 22, 2009 by and among Chelsea Therapeutics International, Ltd., Wedbush Morgan Securities, Inc. and Ladenburg Thalmann & Co. Inc.	8-K	07/23/09	1.1	
1.3	Placement Agency Agreement dated February 26, 2010 by and among the Company, Leerink Swann LLC and Needham & Company, LLC.	8-K	02/26/10	1.1	
1.4	Equity Underwriting Agreement, dated October 1, 2010, between Chelsea Therapeutics International, Ltd. and Deutsche Bank Securities Inc., as representative of the several underwriters.	8-K	10/01/10	1.2	
1.5	Equity Underwriting Agreement, dated February 18, 2011, between Chelsea Therapeutics International, Ltd. and Deutsche Bank Securities Inc., as representative of the several underwriters.	8-K	02/18/11	1.3	
2.1	Agreement and Plan of Merger by and among Ivory Capital Corporation, Chelsea Therapeutics, Inc. and Chelsea Acquisition Corp, dated as of January 17, 2005.	8-K+	01/21/05	2.1	
2.2	Agreement and Plan of Merger between Ivory Capital Corporation and Chelsea Therapeutics International, Ltd., dated as of June 17, 2005.	14A+	07/28/05	Appendix A	
3.1	Certificate of Incorporation for Chelsea Therapeutics International, Ltd., as amended on June 1, 2010	10-Q	11/01/11	3.1	
3.2	Bylaws of Chelsea Therapeutics International, Ltd.	S-1/A	08/18/05	3.2	
4.1	Form of Registered Direct Warrant issued to investors on March 5, 2010.	8-K	02/26/10	4.1	
10.1*	License Agreement dated as of March 24, 2004 between M. Gopal Nair and Chelsea Therapeutics, Inc. (f/k/a Aspen Therapeutics, Inc.)	8-K+	02/16/05	10.1	
10.2	Form of Subscription Agreement for the purchase of Series A Convertible Preferred Stock of Chelsea Therapeutics, Inc.	8-K+	02/16/05	10.3	
10.3	Chelsea Therapeutics International, Ltd. 2004 Stock Plan, as amended, and forms of Notice of Stock Option Grant and Stock Option Agreement, as amended.	10-K	03/12/07	10.4	

<u>Exhibit Number</u>	<u>Description of Document</u>	<u>Registrant's Form</u>	<u>Dated</u>	<u>Exhibit Number</u>	<u>Filed Herewith</u>
10.4	Form of Subscription Agreement and Warrant for the purchase of common stock, par value \$0.0001 per share, of Chelsea Therapeutics International, Ltd.	8-K	02/17/06	10.5	
10.5	Placement Agency Agreement dated November 28, 2005 between Chelsea Therapeutics International, Ltd. and Paramount BioCapital, Inc.	10-K	03/08/06	10.6	
10.6	Employment Agreement between Chelsea Therapeutics International, Ltd. and Dr. Simon Pedder, dated May 1, 2009.	8-K	05/07/09	10.13	
10.7*	Development and Commercialization Agreement dated as of May 5, 2006 between Active Biotech AB and Chelsea Therapeutics International, Ltd.	10-Q	08/14/06	10.8	
10.8*	Exclusive License Agreement effective May 26, 2006 between Dainippon Sumitomo Pharma Co., Ltd. and Chelsea Therapeutics, Inc.	10-Q	08/14/06	10.9	
10.9*	Finder's Agreement dated May 26, 2006 between Paramount BioCapital, Inc. and Chelsea Therapeutics International, Ltd.	10-Q	08/14/06	10.10	
10.10	Form of Subscription Agreement for the purchase of common stock of Chelsea Therapeutics International, Ltd. dated March 19, 2007 and related form of Warrant, dated March 22, 2007.	8-K	03/20/07	10.11	
10.11	Form of Subscription Agreement for the purchase of common stock of Chelsea Therapeutics International, Ltd. dated November 1, 2007.	8-K	11/02/07	10.12	
10.12	Form of Subscription Agreement for the purchase of common stock of Chelsea Therapeutics International, Ltd.	8-K	07/23/09	10.14	
10.13	Form of Subscription Agreement for the purchase of common stock and warrants to purchase common stock of Chelsea Therapeutics International, Ltd.	8-K	02/26/10	10.15	
10.14	Sales Agreement, dated July 2, 2010, between Chelsea Therapeutics, Ltd. and Cantor Fitzgerald & Co.	S-3	01/10/11	10.16	
21.1	Subsidiaries of Chelsea Therapeutics International, Ltd.	10-K	03/12/07	21.1	
23.1	Consent of Independent Registered Public Accounting Firm.				X
23.2	Consent of Independent Registered Public Accounting Firm.				X
31.1	Certification by the Chief Executive Officer pursuant to Section 240.13a-14 or section 240.15d-14 of the Securities and Exchange Act of 1934, as amended.				X

<u>Exhibit Number</u>	<u>Description of Document</u>	<u>Registrant's Form</u>	<u>Dated</u>	<u>Exhibit Number</u>	<u>Filed Herewith</u>
31.2	Certification by the Chief Financial Officer pursuant to Section 240.13a-14 or section 240.15d-14 of the Securities and Exchange Act of 1934, as amended.				X
32.1	Certification by the Chief Executive Officer pursuant to 18 U.S.C. 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X
32.2	Certification by the Chief Financial Officer pursuant to 18 U.S.C. 1350 as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.				X

\* The registrant received confidential treatment with respect to certain portions of this exhibit. Such portions have been omitted from this exhibit and have been filed separately with the SEC.

+ Filed by Ivory Capital Corporation, predecessor in interest.



## Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders  
Chelsea Therapeutics International, Ltd. and Subsidiary

We have audited the accompanying consolidated balance sheets of Chelsea Therapeutics International, Ltd. and Subsidiary (a development stage company) as of December 31, 2010 and 2009, and the related consolidated statements of operations, changes in stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2010, and for the period from April 3, 2002 (inception) through 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. The financial statements for the period from April 3, 2002 (inception) through December 31, 2007, were audited by other auditors whose report dated March 10, 2008 expressed an unqualified opinion on those statements. The financial statements for the period from April 3, 2002 (inception) through December 31, 2007 include total operating expenses and net loss of \$37,144,571 and \$34,685,202, respectively. Our opinion on the consolidated statements of operations, changes in stockholders' equity, and cash flows for the period from April 3, 2002 (inception) through December 31, 2010, insofar as it relates to amounts for prior periods through December 31, 2007, is based solely on the report of other auditors.

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. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, based on our audits and the report of other auditors, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Chelsea Therapeutics International, Ltd. and Subsidiary at December 31, 2010 and 2009, and the consolidated results of their operations and their cash flows for each of the three years in the period ended December 31, 2010, and the period from April 3, 2002 (inception) through December 31, 2010, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Chelsea Therapeutics International, Ltd. and Subsidiary'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 2, 2011, expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Raleigh, North Carolina  
March 2, 2011

## **Report of Independent Registered Public Accounting Firm**

The Board of Directors and Stockholders  
Chelsea Therapeutics International, Ltd.

We have audited the consolidated statements of operations, changes in stockholders' equity and cash flows of Chelsea Therapeutics International, Ltd. and Subsidiary (a development stage company) for the period from April 3, 2002 (inception) to December 31, 2007. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these consolidated 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. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the results of operations and cash flows of Chelsea Therapeutics International, Ltd. and Subsidiary for the period from April 3, 2002 (inception) to December 31, 2007, in conformity with accounting principles generally accepted in the United States of America.

/s/ J.H. Cohn LLP

Roseland, New Jersey  
March 10, 2008

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD. AND SUBSIDIARY**  
**(A Development Stage Company)**

**CONSOLIDATED BALANCE SHEETS**

	<u>December 31,</u> <u>2010</u>	<u>December 31,</u> <u>2009</u>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents .....	\$ 47,593,055	\$ 22,294,649
Short-term investments, net .....	—	11,450,000
Prepaid contract research and manufacturing .....	316,363	293,886
Other prepaid expenses and other current assets .....	246,374	129,687
Total current assets .....	48,155,792	34,168,222
Property and equipment, net .....	180,021	103,795
Other assets .....	38,095	76,950
	<u>\$ 48,373,908</u>	<u>\$ 34,348,967</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable .....	\$ 2,288,241	\$ 2,842,566
Accrued compensation and related expenses .....	1,167,082	894,696
Accrued contract research and manufacturing .....	8,950,469	5,501,329
Other accrued expenses .....	780,352	792,458
Line of credit payable .....	—	11,466,012
Total current liabilities .....	13,186,144	21,497,061
Commitments		
Stockholders' equity:		
Preferred stock, \$0.0001 par value, 5,000,000 shares authorized, no shares issued and outstanding .....	—	—
Common stock, \$0.0001 par value, 100,000,000 and 60,000,000 shares authorized, respectively and 49,790,975 and 33,500,406 shares issued and outstanding, respectively .....	4,979	3,350
Additional paid-in capital .....	168,056,121	108,391,823
Deficit accumulated during the development stage .....	(132,873,336)	(95,543,267)
Total stockholders' equity .....	35,187,764	12,851,906
	<u>\$ 48,373,908</u>	<u>\$ 34,348,967</u>

See accompanying notes to consolidated financial statements.

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD. AND SUBSIDIARY**  
**(A Development Stage Company)**

**CONSOLIDATED STATEMENTS OF OPERATIONS**

	For the years ended December 31,			Period from April 3, 2002 (inception) through December 31, 2010
	2010	2009	2008	
Operating expenses:				
Research and development .....	\$ 30,871,125	\$ 23,985,118	\$ 27,109,174	\$ 108,490,285
Sales and marketing .....	2,476,494	2,289,451	1,561,223	8,956,867
General and administrative .....	4,154,944	4,075,663	3,726,915	19,947,527
Total operating expenses .....	37,502,563	30,350,232	32,397,312	137,394,679
Operating loss .....	(37,502,563)	(30,350,232)	(32,397,312)	(137,394,679)
Interest income .....	242,883	336,850	1,706,568	4,779,691
Interest expense .....	(70,389)	(149,019)	(4,920)	(258,348)
Other income (expense) .....	—	4,390,487	(4,390,487)	—
Net loss .....	\$(37,330,069)	\$(25,771,914)	\$(35,086,151)	\$(132,873,336)
Net loss per basic and diluted share of common stock .....	\$ (0.91)	\$ (0.82)	\$ (1.17)	
Weighted average number of basic and diluted common shares outstanding .....	41,184,623	31,549,739	30,027,031	

**See accompanying notes to consolidated financial statements.**

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD. AND SUBSIDIARY**  
**(A Development Stage Company)**

**CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY**

	Common stock		Additional Paid-In Capital	Unpaid Subscription on common stock	Deferred stock-based compensation	Deficit accumulated during the development stage	Total stockholders' equity
	Shares	Amount					
Issuance of common stock to founders in April 2002 .....	5,428,217	\$ 542	\$ 4,083	\$(4,625)	\$ —	\$ —	\$ —
Balance at December 31, 2003 .....	5,428,217	542	4,083	(4,625)	—	—	—
Common stock issued in March 2004, at approximately \$0.0009 per share, for license fee .....	471,816	47	355	—	—	—	402
Sale and issuance of common stock in April 2004, at approximately \$0.0009 per share to chief executive .....	478,330	48	360	—	—	—	408
Receipt of cash for stock subscription receivable .....	—	—	—	4,625	—	—	4,625
Sale and issuance of common stock in December 2004 at approximately \$2.45 per share, net of issuance costs .....	5,532,994	554	13,550,255	—	—	—	13,550,809
Deferred stock-based compensation ...	—	—	33,525	—	(33,525)	—	—
Amortization of deferred stock-based compensation .....	—	—	—	—	1,529	—	1,529
Net loss .....	—	—	—	—	—	(3,016,559)	(3,016,559)
Balance at December 31, 2004 .....	11,911,357	1,191	13,588,578	—	(31,996)	(3,016,559)	10,541,214
Recapitalization of the Company (See Note 1) .....	457,168	46	(400,046)	—	—	—	(400,000)
Employee stock options exercised .....	14,663	1	998	—	—	—	999
Adoption of SFAS 123R .....	—	—	(31,996)	—	31,996	—	—
Amortization of deferred stock-based compensation .....	—	—	99,319	—	—	—	99,319
Variable accounting for stock options granted to third party .....	—	—	58,594	—	—	—	58,594
Net loss .....	—	—	—	—	—	(7,915,722)	(7,915,722)
Balance at December 31, 2005 .....	12,383,188	1,238	13,315,447	—	—	(10,932,281)	2,384,404
Sale and issuance of common stock with detachable warrants in February 2006 at approximately \$2.77 per share, net of issuance costs .....	7,166,666	717	19,854,935	—	—	—	19,855,652
Common stock issued in March 2006, at par, pursuant to net-share (cashless) exercise of common stock warrants .....	15,461	2	(2)	—	—	—	—
Common stock issued in May 2006, at approximately \$4.35 per share, for license fee .....	63,131	6	274,615	—	—	—	274,621
Employee stock options exercised .....	78,683	8	5,072	—	—	—	5,080
Stock-based compensation .....	—	—	283,983	—	—	—	283,983
Variable accounting for stock options granted to third party .....	—	—	4,192	—	—	—	4,192
Net loss .....	—	—	—	—	—	(8,671,376)	(8,671,376)
Balance at December 31, 2006 .....	19,707,129	1,971	33,738,242	—	—	(19,603,657)	14,136,556

See accompanying notes to consolidated financial statements.

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD. AND SUBSIDIARY**  
**(A Development Stage Company)**

**CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (continued)**

	<u>Common stock</u>		<u>Additional Paid-In Capital</u>	<u>Unpaid Subscription on common stock</u>	<u>Deferred stock-based compensation</u>	<u>Deficit accumulated during the development stage</u>	<u>Total stockholders' equity</u>
	<u>Shares</u>	<u>Amount</u>					
Balance at December 31, 2006 . . . . .	19,707,129	1,971	33,738,242	—	—	(19,603,657)	14,136,556
Common stock issued during 2007, at par, pursuant to net-share (cashless) exercises of common stock warrants . . . . .	68,136	6	(6)	—	—	—	—
Fair value of warrants issued in May 2006 in consideration of finders fee at approximately \$1.75 per share for which vesting was conditioned on an event that occurred in January 2007 . . . . .	—	—	433,750	—	—	—	433,750
Sale and issuance of common stock with detachable warrants in March 2007 at approximately \$4.33 per share, net of issuance costs . . . . .	2,648,306	265	11,476,412	—	—	—	11,476,677
Common stock issued in April 2007, at approximately \$5.63 per share, for license fee . . . . .	26,643	3	149,997	—	—	—	150,000
Common stock issued in June 2007, at \$4.20 per share, pursuant to exercise of common stock warrants, net of fees . . . .	60,000	6	246,994	—	—	—	247,000
Common stock issued in October 2007, at \$4.20 per share, pursuant to exercise of common stock warrants . . . . .	1,200	—	5,040	—	—	—	5,040
Sale and issuance of common stock in November 2007 at approximately \$6.19 per share, net of issuance costs . . . . .	7,388,172	739	45,754,030	—	—	—	45,754,769
Employee stock options exercised . . . . .	17,868	2	15,704	—	—	—	15,706
Stock-based compensation . . . . .	—	—	828,626	—	—	—	828,626
Net loss . . . . .	—	—	—	—	—	(15,081,545)	(15,081,545)
Balance at December 31, 2007 . . . . .	29,917,454	2,992	92,648,789	—	—	(34,685,202)	57,966,579

See accompanying notes to consolidated financial statements.

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD. AND SUBSIDIARY**  
**(A Development Stage Company)**

**CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (continued)**

	<u>Common stock</u>		<u>Additional Paid-In Capital</u>	<u>Unpaid Subscription on common stock</u>	<u>Deferred stock-based compensation</u>	<u>Deficit accumulated during the development stage</u>	<u>Total stockholders' equity</u>
	<u>Shares</u>	<u>Amount</u>					
Balance at December 31, 2007	29,917,454	2,992	92,648,789	—	—	(34,685,202)	57,966,579
Common stock issued during 2008, at par, pursuant to net-share (cashless) exercises of common stock warrants	57,983	6	(6)	—	—	—	—
Common stock issued in 2008, at \$4.20 per share, pursuant to exercise of common stock warrants	11,200	1	47,039	—	—	—	47,040
Final adjustment to issuance costs accrued in conjunction with the sale and issuance of common stock in November 2007 at approximately \$6.19 per share	—	—	5,733	—	—	—	5,733
Common stock issued in April 2008, at approximately \$4.90 per share, for license fee	30,612	3	149,997	—	—	—	150,000
Employee stock options exercised	94,230	9	58,935	—	—	—	58,944
Stock-based compensation	—	—	1,405,752	—	—	—	1,405,752
Net loss	—	—	—	—	—	(35,086,151)	(35,086,151)
Balance at December 31, 2008	30,111,479	3,011	94,316,239	—	—	(69,771,353)	24,547,897
Common stock issued during 2009, at par, pursuant to net-share (cashless) exercises of common stock warrants	63,927	6	(6)	—	—	—	—
Sale and issuance of common stock in July 2009 at approximately \$3.73 per share, net of issuance costs	3,325,000	333	12,402,425	—	—	—	12,402,758
Stock-based compensation	—	—	1,673,165	—	—	—	1,673,165
Net loss	—	—	—	—	—	(25,771,914)	(25,771,914)
Balance at December 31, 2009	33,500,406	3,350	108,391,823	—	—	(95,543,267)	12,851,906

**See accompanying notes to consolidated financial statements.**

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD. AND SUBSIDIARY**  
**(A Development Stage Company)**

**CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (continued)**

	Common stock		Additional Paid-In Capital	Unpaid Subscription on common stock	Deferred stock-based compensation	Deficit accumulated during the development stage	Total stockholders' equity
	Shares	Amount					
Balance at December 31, 2009 . . . . .	33,500,406	3,350	108,391,823	—	—	(95,543,267)	12,851,906
Sale and issuance of common stock with detachable warrants in March 2010 at approximately \$2.50 per share, net of issuance costs . . . . .	6,700,000	670	16,762,253	—	—	—	16,762,923
Sale and issuance of common stock in controlled at-the-market equity offering in September 2010 at approximately \$4.49 per share, net of issuance costs . . . . .	634,500	63	2,851,313	—	—	—	2,851,376
Sale and issuance of common stock in in October 2010 at approximately \$4.60 per share, net of issuance costs . . . . .	8,214,286	821	37,788,721	—	—	—	37,789,542
Common stock issued in 2010 at par, pursuant to net-share (cashless) exercises of common stock warrants . . . . .	676,228	68	(68)	—	—	—	—
Common stock issued in 2010 at \$4.20 per share pursuant to exercise of common stock warrants . . . . .	65,555	7	275,324	—	—	—	275,331
Stock-based compensation . . . . .	—	—	1,986,755	—	—	—	1,986,755
Net loss . . . . .	—	—	—	—	—	(37,330,069)	(37,330,069)
Balance at December 31, 2010 . . . . .	<u>49,790,975</u>	<u>\$4,979</u>	<u>\$168,056,121</u>	<u>\$—</u>	<u>\$—</u>	<u>\$(132,873,336)</u>	<u>\$ 35,187,764</u>

See accompanying notes to consolidated financial statements.

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD. AND SUBSIDIARY**  
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**CONSOLIDATED STATEMENTS OF CASH FLOWS**

	For the years ended December 31,			Period from
	2010	2009	2008	April 3, 2002 (inception) through December 31, 2010
<b>Operating activities:</b>				
Net loss	\$(37,330,069)	\$(25,771,914)	\$(35,086,151)	\$(132,873,336)
Adjustments to reconcile net loss to net cash used in operating activities:				
Non-cash stock-based compensation	1,986,755	1,673,165	1,405,752	6,341,915
Depreciation and amortization	75,610	69,431	57,164	305,514
Stock issued for license fee	—	—	150,000	575,023
Non-cash interest expense	—	—	—	34,020
Other-than temporary impairment (gain on recovery) of short-term and long-term investments	—	(4,390,487)	4,390,487	—
Gain on disposition of fixed assets	—	—	(2,208)	(2,208)
Fair value of warrants for finder's fee	—	—	—	433,750
Changes in operating assets and liabilities:				
Prepaid expenses and other current assets	(139,164)	303,665	(334,676)	(562,737)
Accounts payable, accrued contract research and manufacturing expenses and other accrued expenses	2,882,709	(2,588,850)	7,095,680	12,019,063
Accrued compensation and related expenses	272,386	314,821	12,607	1,167,082
Net cash used in operating activities	(32,251,773)	(30,390,169)	(22,311,345)	(112,561,914)
<b>Investing activities:</b>				
Acquisitions of property and equipment	(151,836)	(14,037)	(175,028)	(487,005)
Proceeds from sale of property and equipment	—	—	3,677	3,677
Redemptions (purchases) of short-term investments, net	11,450,000	14,575,000	2,613,336	—
Security deposits	38,855	—	(63,489)	(38,095)
Net cash provided by (used in) investing activities	11,337,019	14,560,963	2,378,496	(521,423)
<b>Financing activities:</b>				
Proceeds from borrowings from affiliate	—	—	—	1,745,000
(Repayment of) borrowings from line of credit	(11,466,012)	4,188,544	7,277,468	—
Proceeds from exercise of stock options	—	—	58,944	80,729
Proceeds from exercise of common stock warrants	275,331	—	47,040	574,411
Proceeds from sales of equity securities, net of issuance costs	57,403,841	12,402,758	5,733	158,671,627
Recapitalization of the Company	—	—	—	(400,000)
Receipt of cash for stock subscription receivable	—	—	—	4,625
Net cash provided by financing activities	46,213,160	16,591,302	7,389,185	160,676,392
Net increase (decrease) in cash and cash equivalents	25,298,406	762,096	(12,543,664)	47,593,055
Cash and cash equivalents, beginning of period	22,294,649	21,532,553	34,076,217	—
Cash and cash equivalents, end of period	\$ 47,593,055	\$ 22,294,649	\$ 21,532,553	\$ 47,593,055
<b>Supplemental disclosure of cash flow information:</b>				
Cash paid for interest	\$ 70,389	\$ 149,019	\$ 4,920	\$ 224,328

See accompanying notes to consolidated financial statements.

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD. AND SUBSIDIARY**  
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**CONSOLIDATED STATEMENTS OF CASH FLOWS**

**Supplemental disclosure of non-cash investing and financing activities:**

During 2002, the Company issued 5,428,217 shares of its common stock for a subscription receivable of \$4,625.

During 2004, the Company converted a loan with an affiliate for aggregate principal of \$1,745,000 and accrued interest of \$34,020 into shares of its common stock, issuing 677,919 shares, at approximately \$2.62 per share in lieu of repayment of this obligation.

In December 2004, in conjunction with and as compensation for activities related to the December 2004 sale of equity securities, the Company issued warrants to purchase 483,701 shares of its common stock, with a purchase price of approximately \$2.88 per share and an aggregate fair value of \$14,400.

In conjunction with the merger and recapitalization of the Company effective February 11, 2005, the Company issued 11,911,357 shares of its common stock in exchange for all of the issued and outstanding shares of Chelsea Therapeutics, Inc. In addition, in conjunction with and as compensation for facilitating the merger, the Company issued warrants for the purchase of 105,516 shares of its common stock at an exercise price of \$2.62 per share and an aggregate fair value of \$26,700.

In February 2006, in conjunction with and as compensation for activities related to the February 2006 sale of equity securities, the Company issued warrants to purchase 716,666 shares of its common stock, with a purchase price of \$3.30 per share and an aggregate fair value of approximately \$705,000.

In May 2006, in conjunction with and as compensation for activities related to a licensing agreement and under a Finder's Agreement, the Company issued warrants to purchase 250,000 shares of its common stock, with an exercise price of \$4.31 per share. The exercise of these warrants was conditioned on an event that occurred in January 2007 and, accordingly, the Company recorded a charge based on the warrants' fair value determined at January 2007 of \$433,750.

**See accompanying notes to consolidated financial statements.**

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS**

**1. The Company, Basis of Presentation and Summary of Significant Accounting Policies**

***The Company***

Chelsea Therapeutics International, Ltd. (“Chelsea Ltd.” or the “Company”) is a development stage pharmaceutical company focused on the acquisition, development and commercialization of innovative pharmaceutical products. The Company’s currently licensed compounds target a variety of prevalent medical conditions, particularly rheumatoid arthritis, psoriasis, cancer, other immunological disorders, neurogenic orthostatic hypotension associated with Parkinson’s Disease and other autonomic disorders. The Company’s operating subsidiary, Chelsea Therapeutics, Inc. (“Chelsea Inc.”), was incorporated in the State of Delaware on April 3, 2002 as Aspen Therapeutics, Inc., with the name changed in July 2004. In February 2005, Chelsea Inc. merged with a wholly-owned subsidiary of Chelsea Ltd.’s predecessor company, Ivory Capital Corporation (“Ivory”), a Colorado public company with no operations (the “Merger”). The Company reincorporated into the State of Delaware in July 2005, changing its name to Chelsea Therapeutics International, Ltd.

As a result of the Merger of Ivory and Chelsea Inc. in February 2005, and the reincorporation in Delaware in July 2005, Chelsea Ltd. is the reporting company and is the 100% owner of Chelsea Inc. The separate existence of Ivory ceased in connection with the Delaware reincorporation in July 2005. Except where the context provides otherwise, references to the “Company” and similar terms mean Ivory, Chelsea Ltd. and Chelsea Inc.

***Basis of Presentation***

Since inception, the Company has focused primarily on organizing and staffing, negotiating in-licensing agreements with partners, acquiring, developing and securing its proprietary technology, participating in regulatory discussions with the United States Food and Drug Administration, or FDA, the European Medicines Agency, or EMA and other regulatory agencies and undertaking preclinical trials and clinical trials of product candidates. The Company is a development stage company and has generated no revenue since inception.

The Company has sustained operating losses since its inception and expects such losses to continue over the next several years. Management plans to continue financing the Company’s operations with equity issuances, debt arrangements, strategic alliances or other arrangements of a collaborative nature. If adequate funds are not available, the Company may be required to delay, reduce the scope of, or eliminate one or more of its research or development programs, delay certain activities, or limit or cease operations in which event its business, financial condition and results of operations would be materially harmed.

For presentation purposes, the Company has restated all information contained in this report related to shares authorized, issued and outstanding and related disclosures of weighted average shares and loss per share to reflect the results of the Delaware reincorporation in July 2005 as if the Delaware reincorporation had occurred at the beginning of each of the periods presented.

***Basis of Consolidation***

The accompanying financial statements present, on a consolidated basis, the financial position and results of operations of Chelsea Ltd. and its subsidiary. All significant intercompany transactions and balances have been eliminated in consolidation.

***Use of Estimates***

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)**

amounts of assets and liabilities and the disclosure of contingent liabilities at the date of the financial statements as well as the reported revenues and expenses during the reporting periods. On an ongoing basis, management evaluates its estimates and judgments. Management bases estimates on its historical experience and on various other factors that it believes are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

***Cash and Cash Equivalents***

Cash and cash equivalents consist of cash and other highly-liquid investments with maturities of three months or less at the date of purchase.

***Short-Term Investments***

Short-term investments consisted of investments in auction rate securities, or ARS. ARS are generally long-term debt instruments for which interest rates are reset through a Dutch auction process that occurs at pre-determined calendar intervals, generally each 28 or 35 days. All of the Company's investments in ARS were classified as trading securities at December 31, 2009 and were redeemed as planned under an executed settlement agreement on June 30, 2010. The Company elected the fair value option in accounting for its trading securities and, accordingly, accounted for such investments at their determined fair value, with changes in the fair value recorded in the statement of operations.

***Concentration of Credit Risk***

Financial instruments that potentially subject the Company to a significant concentration of credit risk consist primarily of cash and cash equivalents and short-term investments. The Company maintains deposits in federally insured financial institutions that, under the Temporary Liquidity Guarantee Program, or TLGP, through December 31, 2010, were fully insured by the Federal Deposit Insurance Corporation, or FDIC. Subsequently, the FDIC implemented its Transaction Account Guarantee program that will fully insure such deposits until December 31, 2012. The Company continues to maintain deposits in excess of federally insured amounts in commercial checking accounts and interest-bearing money market accounts. However, while giving consideration to the expiration of the TLGP at December 31, 2010, management believes the Company is not exposed to significant credit risk for its cash and cash equivalents due to the financial position of the depository institutions in which those deposits are held and the nature of the investments.

***Fair Value of Financial Instruments***

The carrying value of the Company's financial instruments, including cash and cash equivalents and accounts payable approximates fair value given their highly-liquid and short-term nature.

For financial assets and liabilities and any other assets and liabilities carried at fair value, the Company completes analyses of fair value and provides certain disclosures about fair value measurements. Fair value is based on the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. Under the fair value hierarchy that prioritizes observable and unobservable inputs used to measure fair value, the Company performs analyses on a consistent basis and designs its disclosures surrounding such analyses and the fair value determined at the balance sheet date to meet required presentation and disclosure requirements.

**CHELSEA THERAPEUTICS INTERNATIONAL, LTD. AND SUBSIDIARY**  
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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)**

***Property and Equipment***

Property and equipment, which consists of furniture and fixtures, software and equipment, is stated at cost and depreciated or amortized using the straight-line method over the estimated useful lives of the related assets. The useful life for all classes of assets other than leasehold improvements is three years. The useful life for leasehold improvements is the shorter of the expected life of the leasehold improvement or the remaining term of the lease.

***Impairment of Long-Lived Assets***

The Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. The impairment loss, if recognized, would be based on the excess of the carrying value of the impaired asset over its respective fair value. Impairment, if any, is assessed using undiscounted cash flows. Through December 31, 2010, there has been no such impairment.

***Research and Development***

Research and development expenditures are expensed as incurred. The Company often contracts with third parties to facilitate, coordinate and perform agreed upon research and development activities. To ensure that research and development costs are expensed as incurred, the Company measures expense based on work performed for the underlying contract, typically utilizing a percentage-of-completion approach, and records prepaid assets or accrues expenses on a monthly basis for such activities based on the measurement of liability from expense recognition and the receipt of invoices.

These contracts typically call for the payment of fees for services at the initiation of the contract and/or upon the achievement of certain milestones. In the event that the Company prepays fees for future milestones, it records the prepayment as a prepaid asset and amortizes the asset into research and development expense over the period of time the contracted research and development services are performed. Most fees are incurred throughout the contract period and are expensed based on their percentage of completion at a particular date.

These contracts generally include pass through fees. Pass through fees include, but are not limited to, regulatory expenses, investigator fees, travel costs, and other miscellaneous costs including shipping and printing fees. Because these fees are incurred at various times during the contract term and they are used throughout the contract term, the Company records an estimated monthly expense allocation to recognize the fees during the contract period. Fees incurred to set up the clinical trial are expensed during the setup period.

Costs related to the acquisition of technology rights and patents for which development work is still in process are expensed as incurred and considered a component of research and development costs.

The Company has contracted with a third-party to manufacture commercial quantities of Northera prior to the date it anticipates that Northera will receive final regulatory marketing approval and might perform similar activities with other product candidates in the future. The scale-up and commercial production of pre-launch inventories involves the risk that such products may not be approved for marketing by the appropriate regulatory agencies on a timely basis, or ever. As such, until final approval to market any of the Company's product candidates is received from the appropriate regulatory agencies, such costs are expensed to research and development.

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)**

***Loss per Share***

Basic net loss per common share is calculated by dividing net loss by the weighted-average number of common shares outstanding for the period, without consideration for potentially dilutive securities. For the periods presented, basic and diluted net loss per common share are identical as potentially dilutive securities from stock options and stock warrants would have an antidilutive effect since the Company incurred a net loss. The number of shares of common stock potentially issuable at December 31, 2010, 2009 and 2008 upon exercise or conversion that were not included in the computations of net loss per share were 9,917,518, 7,873,688 and 7,055,089, respectively.

***Income Taxes***

The Company determines deferred tax assets or liabilities based on the difference between the financial statement and the tax bases of assets and liabilities as measured by the enacted tax rates, which will be in effect when these differences reverse. The Company provides a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized.

The Company also recognizes, in its consolidated financial statements, the impact of a tax position if that position is more likely than not to be sustained upon examination, based on the technical merits of the position and provides explicit disclosure about the Company's uncertainties related to the income tax position, including a detailed roll-forward of tax benefits taken that do qualify for financial statement recognition.

***Stock-Based Compensation***

The Company accounts for its stock options using a fair value based method of accounting for stock options or similar equity instruments and requires the measurement and recognition of compensation expense for all share-based payment awards made to employees and non-employee directors based on estimated fair values determined using an option-pricing model. The value of the portion of the award that is ultimately expected to vest is recognized as expense over the requisite service periods in the Company's statements of operations.

The fair value of each option award made to employees and directors during the years ended December 31, 2010, 2009 and 2008 was estimated on the date of grant using the Black-Scholes closed-form option valuation model utilizing the assumptions noted in the following table. To determine the risk-free interest rate, the Company utilized the U.S. Treasury yield curve in effect at the time of grant with a term consistent with the expected term of the Company's awards. The Company estimated the expected life of the options granted based on anticipated exercises in future periods assuming the success of its business model as currently forecasted. The expected dividends reflect the Company's current and expected future policy for dividends on its common stock. To determine the expected stock price volatility for stock options, the Company examined historical volatilities for industry peers closely related to the current status of its business, but with sufficient trading history to be able to determine volatility. Utilizing a weighted average calculation to account for the limited price history of the Company's stock, an analysis of the historical volatility of its stock price in combination with the historical volatility of the industry peers selected was used to determine an appropriate volatility factor. The Company plans to continue to analyze the expected stock price volatility and expected term assumption at each grant date as more historical data for its common stock becomes available. . Given the Company's low historical rate of attrition and the senior nature of the roles for a significant portion of the Company's employees, the Company estimated that it would experience no forfeitures or that the rate of forfeiture would be immaterial to the recognition of compensation expense for those options currently outstanding. Due to the limited amount of

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)**

historical data available to the Company, particularly with respect to stock-price volatility, employee exercise patterns and forfeitures, actual results could differ from the Company's assumptions. The table below summarizes the assumptions utilized in estimating the fair value of the stock options granted during the years ended December 31, 2010, 2009 and 2008:

	<u>For the years ended December 31,</u>		
	<u>2010</u>	<u>2009</u>	<u>2008</u>
Weighted-average risk-free interest rate . . . . .	2.39%	1.75%	2.95%
Weighted-average expected life of options . . . . .	5 years	5 years	5 years
Expected dividend yield . . . . .	0%	0%	0%
Weighted-average expected volatility . . . . .	93.95%	82.71%	63.64%

The Company records compensation expense on a straight-line method over the vesting period of its options and recorded compensation expense of \$1,986,755, \$1,673,165 and \$1,405,752 for the years ended December 31, 2010, 2009 and 2008, respectively, in conjunction with option grants made to employees and non-employee directors. As of December 31, 2010, the Company had total unrecognized compensation expense related to options granted to employees and non-employee directors of approximately \$3.0 million, which will be recognized over a weighted-average remaining period of two years. The expected future amortization expense for unrecognized compensation expense for stock option grants to employees and non-employee directors at December 31, 2010 is as follows:

Year ending December 31, 2011 . . . . .	\$1,535,943
Year ending December 31, 2012 . . . . .	903,881
Year ending December 31, 2013 . . . . .	544,321
Year ending December 31, 2014 . . . . .	47,401
	<u>\$3,031,546</u>

To date, option awards to consultants, advisors or other independent contractors have been granted with an exercise price equal to the market price of the Company's stock at the date of the grant, have 10-year contractual terms and vest dependent upon the completion of performance commitments. As such, the value of stock options is measured at the then-current market value as of financial reporting dates and compensation cost is recognized for the net change in the fair value of the options for the reporting period, until such performance commitments are met. Once each commitment is met, the options that vest in association with that commitment are adjusted, for the last time, to the then-current fair value and compensation cost is recognized accordingly (see Note 7).

In determining the fair value of options granted to consultants, advisors and other independent contractors, the Company uses the Black-Scholes closed-form option valuation model in a manner consistent with its use in determining the fair value of options granted to employees and directors. However, the expected life of the options is based on the contractual lives as defined in agreements with the third parties. No such grants were made during 2010, 2009 or 2008.

**2. Auction Rate Securities**

On December 31, 2009, the Company held total investments in auction rate securities, or ARS, with a par value of approximately \$11.45 million, classified as trading securities and held at UBS Financial Services, Inc., or UBS. The Company's ARS investments represented interests in collateralized debt obligations supported by

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pools of student loans and none were collateralized by mortgage, credit card or insurance securitizations. During 2008, the Company finalized the details of its settlement agreement related to those ARS held at UBS and accepted the terms for ARS Rights (the “ARS Rights”) for the illiquid ARS holdings maintained at UBS as of February 13, 2008. The ARS Rights provided the Company with the ability to sell the ARS, along with the ARS Rights, to UBS at the par value of the ARS no earlier than June 30, 2010 and were to expire on July 2, 2012. The ARS Rights granted UBS the sole discretion and right to sell or otherwise dispose of ARS at any time up until June 30, 2010, so long as the holder received a payment of par upon any sale or disposition. The ARS Rights were not transferable, not tradable and were not quoted or listed on any securities exchange or any other trading network.

In addition, UBS also agreed that an affiliate would provide the Company with a no net-cost line of credit. Under the terms of the line of credit agreements the Company received funds in December 2008 and March 2009 equivalent to 100% of the par value of the Company’s ARS investments, providing the Company with full liquidity for all its investments in ARS held with UBS. The line of credit agreements also stipulated that proceeds from liquidation of the ARS through redemption or otherwise, would first be applied to the balance outstanding on the line of credit. The Company exercised the ARS Rights on June 30, 2010 and, after applying the proceeds of the redemptions of those ARS Rights, had no remaining investment in ARS or any liability under the line of credit as of the date of exercise.

In 2008, recognizing that the ARS Rights act as an economic hedge against any further price movement in those ARS holdings, the Company elected to account for the ARS Rights under the fair value option to mitigate volatility in reported earnings due to the relationship between the ARS Rights and the ARS. The Company adjusted the ARS Rights to fair value at each financial statement date with corresponding changes in fair value reported in earnings. Simultaneously, the Company elected a one-time transfer of the ARS covered under the settlement agreement with UBS from the available-for-sale category to the trading category recognizing the unprecedented failure of the entire market for ARS. This election allowed any movements in the fair value of the ARS to be reported in earnings, creating relative accounting symmetry with the ARS Rights until the settlement was realized. The ARS Rights were recorded at fair value and classified as short-term investments as of December 31, 2009.

As a result of its continuing analysis of fair value, the Company recorded no additional trading loss in 2010 related to its trading securities or any corresponding adjustment to the fair value of its ARS Rights, prior to redemption on June 30, 2010. During the year ended December 31, 2009, the Company recorded a gain of approximately \$4.1 million from the recovery of the other-than-temporary impairment that the Company had recorded against investments with an aggregate par value of \$11.6 million, classified as available-for-sale, that were redeemed during 2009. Also, during the year ended December 31, 2009, the Company recorded a gain of approximately \$0.2 million related to the increased value of the ARS Rights due to the additional funding received under the line of credit and the resulting elimination of any performance risk associated with the settlement. In addition, the Company recorded the recovery of \$0.1 million of previously recorded other-than-temporary impairment losses related to \$0.3 million in partial redemptions at par of its available-for-sale ARS investments during 2009.

At December 31, 2008, the Company held short-term and long-term investments in ARS, recorded at fair value, of \$10.3 million and \$11.3 million, respectively, with an aggregate par value of approximately \$26 million. Based on the Company’s estimate of the fair value and information provided by a third party expert engaged to assist the Company in valuing its holdings at Banc of America Securities, the Company recorded an other-than-temporary impairment loss for the year ended December 31, 2008 of approximately \$4.1 million related to these securities. In addition, the Company recorded other-than-temporary impairment losses related to

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)**

its trading securities that were then classified as available-for-sale securities and held at UBS, of approximately \$2.2 million during the year ended December 31, 2008. Offsetting these impairment charges, the Company recorded other income and a corresponding long-term asset for the fair value of the ARS Rights obtained from UBS in November 2008 of \$2.0 million. In the aggregate, the recording of the gain from the ARS Rights and the recognition of other-than-temporary impairment losses resulted in approximately \$0.2 million of net expense impact on the consolidated statement of operations.

**3. Fair Value Measurements**

In determining fair value, the Company utilizes techniques that optimize the use of observable inputs, when available, and minimize the use of unobservable inputs to the extent possible. As normal trading activity within public markets for ARS ceased during the quarter ended March 31, 2008 and had not resumed with any regularity through 2010, there was an absence of observable market quotes (level 1 inputs). Trading activity in the secondary markets for ARS was not sufficiently active and the resulting data did not qualify as appropriate level 2 inputs. Data points that were available did not technically qualify as level 2 inputs and were characterized as unobservable (level 3) inputs, along with other inputs including fair value information provided by UBS on the Company's ARS holdings with UBS (based on percentage of collateralization, assessments of counterparty credit quality, default risk underlying the security, the mix of Federal Family Education Loan Program, or FFELP, loans and private loans) and overall capital market liquidity.

At December 31, 2010, with the redemption of the Company's ARS investments (see Note 2), assets measured at fair value on a recurring basis consist only of cash and cash equivalents of approximately \$47.6 million. Based on the short-term liquid nature of these assets, the fair value, determined using level 1 inputs, is equivalent to the recorded book value.

**4. Property and equipment:**

Property and equipment consist of the following:

	December 31,	
	2010	2009
Furniture and fixtures . . . . .	\$ 186,119	\$ 156,249
Software . . . . .	42,569	19,046
Leasehold improvements . . . . .	24,142	24,142
Computer and office equipment . . . . .	202,935	104,493
	455,765	303,930
Less—accumulated depreciation and amortization . . . . .	(275,744)	(200,135)
	\$ 180,021	\$ 103,795

Depreciation and amortization expense was \$75,610, \$69,431 and \$57,164 for the years ended December 31, 2010, 2009 and 2008, respectively.

**5. Common Stock Offerings**

On October 6, 2010, the Company raised gross proceeds of approximately \$40.3 million through the sale of 8,214,286 shares of its common stock in a publicly-marketed offering. These shares were offered pursuant to the Company's shelf registration statement, as amended effective October 1, 2010 pursuant to Rule 462(b) to

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)**

increase the dollar amount of securities available for sale, as filed with the SEC under which it may offer shares of its common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of \$61,566,686. Such registration statement became effective as of August 20, 2009.

In July 2010, the Company filed the required documents and became eligible to use an at-the-market common equity sales program for the sale of up to 3,000,000 shares of common stock. In September 2010, the Company sold 634,500 shares of common stock under this program resulting in net proceeds, after expenses, of approximately \$2.9 million, or \$4.49 per share. These shares were offered pursuant to the Company's 2009 shelf registration statement.

On March 5, 2010, the Company raised gross proceeds of approximately \$18.2 million through the sale of 6,700,000 shares of its common stock plus warrants for the purchase of 2,345,000 shares of its common stock (the "2010 Offering"). These warrants had an aggregate fair value of approximately \$3.9 million, permit the holders to purchase the underlying common shares at \$2.79 each or elect a net share settlement and are exercisable in whole at any time, or in part from time to time, during the period commencing six months after the date of issuance and ending three years from the date of issuance. These shares were offered pursuant to the Company's 2009 shelf registration statement. In connection with this offering, the Company paid commissions and other offering-related costs of approximately \$1.5 million.

There are no more securities available under the Company's 2009 shelf registration.

On July 28, 2009, the Company raised gross proceeds of approximately \$13.3 million through the sale of 3,325,000 shares of its common stock. These shares were offered pursuant to the Company's prior shelf registration statement, as amended effective July 22, 2009 pursuant to Rule 462(b) to increase the dollar amount of securities available for sale, as filed with the SEC under which the Company could offer shares of its common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of \$62,218,060. Such registration statement became effective as of October 11, 2007. In connection with the July 2009 offering, the Company received net proceeds, after deducting placement fees and offering expenses, of approximately \$12.4 million.

On November 8, 2007, the Company raised gross proceeds of approximately \$48.9 million through the sale of 7,388,172 shares of its common stock in a registered direct offering. These shares were offered pursuant to the Company's 2007 shelf registration statement. In connection with this offering, the Company paid commissions and recorded or accrued other offering-related costs of approximately \$3.2 million.

There are no more securities available under the Company's 2007 shelf registration.

On March 22, 2007, the Company raised gross proceeds of approximately \$12.5 million through the sale of 2,648,306 shares of its common stock plus warrants for the purchase of 794,492 shares of its common stock (the "2007 Placement"). The aggregate fair value of these warrants was approximately \$1.3 million. The warrants permit the holders to purchase the underlying common shares at \$5.66 each and are exercisable in whole at any time, or in part from time to time, for cash, for five years from the date of issuance. The warrants are redeemable at par value at the Company's option in the event that the volume weighted-average closing price of the Company's common stock is greater than \$12.00 per share for any 20 consecutive trading days provided the Company gives 60 business days' written notice to the holders and simultaneously call all warrants on the same terms. Under the terms of the 2007 Placement, the Company agreed to and filed a registration statement with the

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SEC within 30 days of the closing for the shares of common stock sold and the shares of common stock underlying the warrants and such registration became effective on August 7, 2007. In connection with this offering, the Company paid commissions and other offering-related costs of approximately \$1.0 million in cash.

On February 13, 2006, the Company raised gross proceeds of approximately \$21.5 million through the sale of 7,166,666 shares of its common stock plus warrants for the purchase of 2,149,999 shares of its common stock (the “2006 Placement”). The allocated aggregate fair value of these warrants was approximately \$1.1 million. The warrants permitted the holders to purchase the underlying common shares, for cash only, at \$4.20 each and were exercisable in whole at any time, or in part from time to time, for five years from the date of issuance. (See Note 10) The warrants were redeemable at par value at the Company’s option in the event that the Company’s volume weighted-average closing bid price of its common stock was greater than \$9.00 per share for any 20 consecutive trading days provided that the Company gave 30 business days’ written notice to the holders and simultaneously called all warrants on the same terms. In connection with the 2006 Placement, the Company paid commissions and other offering-related costs of approximately \$1.6 million in cash and issued warrants to the placement agent for the purchase of 716,666 shares of the Company’s common stock with an exercise price of \$3.30 per share, or 110% of the price of the shares sold in the offering and an aggregate fair value of approximately \$0.7 million. These warrants are exercisable in whole at any time, or in part from time to time, for cash or in a net share settlement, for seven years from the date of issuance. Under the terms of the 2006 Placement, the Company agreed to and filed a registration statement with the SEC within 30 days of the closing for the shares of common stock sold and the shares of common stock underlying the warrants and such registration became effective on March 29, 2006.

In December 2004, Chelsea, Inc. raised gross proceeds of approximately \$14.5 million through the sale of 5,532,994 shares of its common stock (the “2004 Placement”). The amount raised includes the conversion of a \$1.7 million stockholder loan along with accrued interest, for which a total of 677,919 shares of common stock were issued. In connection with this offering, Chelsea, Inc. paid commissions and other offering-related costs of approximately \$1.0 million in cash and issued warrants to the placement agent for the purchase of 483,701 shares of its common stock with an aggregate fair value of approximately \$14,000. The warrants permit the holders to purchase the underlying common shares at \$2.88 per share, and are exercisable in whole at any time, or in part from time to time, for cash or in a net share settlement, for seven years from the date of issuance.

## **6. Commitments**

### ***Facility Lease***

On October 21, 2010, the Company entered into an amendment to its lease agreement, dated March 7, 2008, to increase the office space in Charlotte, North Carolina that serves as its corporate headquarters. Occupancy of the additional space is expected on or around March 11, 2011. Occupancy for the originally leased space occurred on or about May 15, 2008. Upon taking delivery of the newly added space and upon expiration of a free rental period of six months from the date of delivery anticipated on or about September 11, 2011, the monthly payments will increase by approximately \$8,000 per month to a total of approximately \$28,000. The lease, as amended, expires on or about March 11, 2016 and calls for annual rent increases of 3%. A security deposit of approximately \$38,000 is being held by the lessor in conjunction with the lease. In addition, the lease initially provided an option to rent additional adjacent space. Such option expired in November 2009. The future aggregate minimum lease payments under non-cancellable operating leases are approximately \$1.8 million through the lease expiration date of March 2016.

The Company leased its former corporate headquarters under an operating lease, as amended, that expired in June 2008. The lease contained no provisions for renewal periods of any fixed lengths.

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Rent expense for the years ended December 31, 2010, 2009 and 2008 was \$202,267, \$248,404 and \$179,614, respectively.

***License Agreements***

In March 2004, the Company entered into a license agreement with Dr. M. Gopal Nair, Ph.D., of the University of South Alabama College of Medicine, for the rights to use, produce, distribute and market products derived from an invention by Dr. Nair, claimed in US Patent # 5,912,251, entitled “metabolically inert anti-inflammatory and antitumor antifolates”, designated by the Company as CH-1504 and related compounds. The license provides the Company exclusive, worldwide (excluding India) rights for CH-1504 and related compounds. The Company made an upfront payment in May 2004 of \$150,000 and milestone payments as required by the agreement of \$100,000 each in March 2006 and 2005. In April 2007, the Company issued 26,643 shares of its common stock, subject to trading restrictions, at a value of approximately \$5.63 per share, in settlement of the \$150,000 annual milestone payment liability. In March 2008, the Company made a milestone payment of \$100,000 related to patient dosing in a Phase II study as required by the agreement. In April 2008, the Company issued 30,612 shares of its common stock, subject to trading restrictions, at a value of approximately \$4.90 per share, in settlement of the 2008 anniversary milestone payment. In April 2009, the Company made the 2009 anniversary milestone payment of \$150,000. In September 2010, the Company accrued a milestone payment of \$100,000 related to patient dosing in a Phase II study as required by the agreement. The Company is obligated to pay royalties under the agreement until the later of the expiration of the applicable patent or the applicable last date of market exclusivity after the first commercial sale, on a country-by-country basis. There are no minimum royalties required under the agreement. The Company is also obligated to make future potential milestone payments based on the achievement of specific development and regulatory approval milestones. Based on the Company’s current development plans for compounds licensed under this agreement, approximately \$1.5 million of payments may become due if specific milestones are achieved, subject to the Company’s right to terminate the license agreement. In addition, should the Company enter into an out-licensing agreement, such payments could be offset by revenue received from the sub-licensee.

In May 2006, the Company entered into an agreement with Dainippon Sumitomo Pharma Co., Ltd. (“DSP”) for a worldwide, exclusive, sub-licensable license and rights to certain intellectual property and proprietary information (the “DSP Agreement”) relating to L-threo-3,4-dihydroxyphenylserine (“L-DOPS” or “droxidopa”) including, but not limited to all information, formulations, materials, data, drawings, sketches, designs, testing and test results, records and regulatory documentation. As consideration for these rights, the Company paid DSP \$100,000 and issued 63,131 shares of its common stock, with a value of approximately \$4.35 per share, or \$274,621. As additional consideration, the Company agreed to pay DSP and/or its designees (1) royalties on the sales should any compound be approved for commercial sale, and (2) milestone payments, payable upon achievement of milestones as defined in the DSP Agreement. In February 2008, the Company made a milestone payment under the DSP Agreement of \$500,000 related to patient dosing in a Phase III study and has remaining potential future milestone payments, subject to the Company’s right to terminate the DSP Agreement, totaling \$3.25 million. The Company and DSP also initiated, and the Company agreed to fund, activities focused on modifying the manufacturing capabilities of DSP in order to expand capacity and comply with regulations and requirements of the FDA. Based on work performed by DSP as of December 31, 2010, the Company had recorded expense of approximately \$3.3 million and had a remaining liability of \$0.4 million at December 31, 2010.

In conjunction with and as consideration for activities related to the execution of the DSP Agreement, the Company entered into a Finder’s Agreement with Paramount BioCapital, Inc. (“Paramount”). In May 2006, pursuant to the Finder’s Agreement, the Company issued warrants for the purchase of 250,000 shares of its

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common stock at an exercise price of \$4.31 per share. The exercise of these warrants was conditioned on an event that occurred in January 2007 and, accordingly, the Company recorded a charge for the fair value of the warrants at January 2007 of \$433,750. The Company utilized the Black-Scholes-Merton valuation model for estimating the fair value of the warrants at the date the condition lapsed, based on a risk-free interest rate of 4.79%, an expected life of three years, an expected dividend yield of 0%, an expected volatility of 66.01% and no estimated forfeitures. As additional consideration, the Company agreed to (1) make future milestone payments to Paramount, upon achievement of milestones as defined in the Finder's Agreement, (2) pay royalties on sales should any licensed compound become available for commercial sale, and (3) compensate a stated third-party consultant for services rendered in the evaluation of the transaction with DSP. The Company has remaining potential future milestone payments under the Finder's Agreement of \$150,000.

The amount expended under these agreements and charged to research and development expense was \$100,000 during the year ended December 31, 2010, \$150,000 during the year ended December 31, 2009 and \$750,000 during the year ended December 31, 2008.

***Development and Commercialization Agreement***

Effective May 2006, the Company entered into a development and commercialization agreement (the "Development Agreement") with Active Biotech AB ("AB") to co-develop and commercialize the I-3D portfolio of orally active, dihydroorotate dehydrogenase ("DHODH") inhibiting compounds for the treatment of autoimmune diseases and transplant rejection. Under the terms of the Development Agreement, an initial payment of \$1.0 million was made to AB at the time of the Development Agreement with such funds utilized to cover the initial costs of research and development efforts jointly approved by both parties. At December 31, 2006, the Company had expensed the entire \$1.0 million payment and expensed additional costs of \$0.3 million. During 2007, the Company expensed costs of \$0.6 million under the program related to costs of research and development. During 2008, the Company and AB ceased joint discovery efforts on this portfolio.

In April 2008, the Company and AB entered into a termination and assignment agreement (the "Termination Agreement"), whereby AB discontinued its participation in the I-3D co-development program and assigned its entire right, title and interest in the portfolio to the Company in exchange for royalties on future sales. The Termination Agreement also eliminated the Company's obligation related to payment of potential future development milestones under the Development Agreement. The Company has recorded no costs related to this program during 2010, 2009 or 2008.

***Contract Research and Manufacturing Purchase Obligations***

The Company often contracts with third parties to facilitate, coordinate and perform agreed upon research and development and manufacturing activities. These contracts typically call for the payment of fees for services at the initiation of the contract and/or upon the achievement of certain milestones. The Company currently intends to continue its research and manufacturing activities as contracted at December 31, 2010. However, there can be cancellation fees associated with these contracts that could be punitive in nature.

In addition, the Company has contracted with a third party for the manufacture of commercial quantities of Northera prior to the date it anticipates that Northera will receive final marketing approval and might perform similar activities for other of its product candidates in the future. The scale-up and commercial production of pre-launch inventories involves the risk that such products may not be approved for marketing by the appropriate regulatory agencies on a timely basis, or ever. This risk notwithstanding, the Company initiated such activities with its primary supplier of active pharmaceutical ingredient of Northera in December 2010 and had accrued

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expenses of approximately \$1.9 million related to these activities at December 31, 2010. Until final approval to market any of the Company's product candidates is received from the appropriate regulatory agencies, such costs are expensed to research and development. The Company intends to continue such activities during 2011 in order to carry out validation activities and build pre-launch inventories of Northera prior to final governmental approval.

Commitments under research and development programs and pre-launch commercial inventory activities represent contractual commitments entered into for materials and services in the normal course of business and totaled approximately \$21.5 million at December 31, 2010.

### **7. Stockholders' Equity**

On June 1, 2010, the Company's Certificate of Incorporation was amended to increase the number of authorized shares of capital stock from 65,000,000 shares to 105,000,000 shares and to increase the number of authorized shares of common stock from 60,000,000 shares to 100,000,000 shares.

#### ***Preferred Stock***

The Company's Certificate of Incorporation provides that the Board of Directors of the Company has the authority to issue up to an aggregate of 5,000,000 shares of preferred stock in one or more classes or series and to determine, with respect to any such class or series, the designations, powers, preferences and rights of such class or series, and the qualifications, limitations and restrictions thereof, including dividend rights, dividend rates, conversion rights, voting rights, terms of redemption (including sinking fund provisions), redemption prices, liquidation preferences and the number of shares constituting any class or series or the designation of such class or series, without further vote or action by the stockholders.

As of December 31, 2010, no shares of preferred stock were issued and outstanding.

#### ***Common Stock***

In April 2008, the Company issued 30,612 shares of its common stock, subject to trading restrictions, at a value of approximately \$4.90 per share, as consideration for the \$150,000 anniversary milestone payment due under its product license agreement with Dr. M. Gopal Nair (see Note 6).

In April 2007, the Company issued 26,643 shares of its common stock, subject to trading restrictions, at a value of approximately \$5.63 per share, as consideration for the \$150,000 anniversary milestone payment due under its product license agreement with Dr. M. Gopal Nair (see Note 6).

In May 2006, the Company issued 63,131 shares of its common stock as consideration for a product license agreement with DSP (see Note 6), with a value of approximately \$4.35 per share, or \$274,621.

During April 2004, the Company issued 471,816 common shares as consideration in the product license agreement (see Note 6) and 478,330 shares were sold to Simon Pedder, the Company's President and Chief Executive Officer under the terms of his employment agreement. These shares were valued at what was, at that time, Chelsea's common stock's estimated aggregate fair value of \$402 and \$408, respectively, with such nominal values reflecting an asset-based valuation methodology.

During 2002, the Company issued 5,428,217 shares of its common stock for a subscription receivable of \$4,625.

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***Warrants***

At December 31, 2010 and 2009, the Company had outstanding warrants to purchase 5,255,588 and 4,060,758 shares, respectively, of the Company's common stock at prices ranging from \$2.62 to \$5.66 per share.

On March 5, 2010, in conjunction with the 2010 Offering, the Company issued warrants for the purchase of 2,345,000 shares of its common stock. These warrants had an aggregate fair value of approximately \$3.9 million, permit the holders to purchase the underlying common shares at \$2.79 each or elect a net share settlement and are exercisable in whole at any time, or in part from time to time, during the period commencing six months after the date of issuance and ending three years from the date of issuance.

In March 2007, in conjunction with the 2007 Placement (see Note 5), the Company issued warrants for the purchase of 794,492 shares of its common stock. The aggregate fair value of these warrants was approximately \$1.3 million. The warrants permit the holders to purchase the underlying common shares at \$5.66 each and are exercisable in whole at any time, or in part from time to time, for cash, for five years from the date of issuance. The warrants are redeemable at par value at the Company's option in the event that the volume weighted-average closing price of the Company's common stock is greater than \$12.00 per share for any 20 consecutive trading days provided the Company gives 60 business days' written notice to the holders and simultaneously call all warrants on the same terms.

In May 2006, in conjunction with and as compensation for activities related to the product license agreement with DSP (see Note 6) and under a finder's agreement, the Company issued warrants to purchase 250,000 shares of its common stock, with an exercise price of \$4.31 per share. The exercise of these warrants was conditioned on an event that did not occur until January 2007. As such, in January 2007, the Company recorded a charge based on the warrants' aggregate fair value at that date of \$433,750. The warrants permit the holders to purchase the underlying common shares at \$4.31 per share, and are exercisable in whole at any time, or in part from time to time, for cash or in a net share settlement, for seven years from the date of issuance.

In February 2006, in conjunction with the 2006 Placement (see Note 5), the Company issued warrants for the purchase of 2,149,999 shares of its common stock. The allocated aggregate fair value of these warrants was approximately \$1.1 million. The warrants permitted the holders to purchase the underlying common shares at \$4.20 each and are exercisable in whole at any time, or in part from time to time, for cash, for five years from the date of issuance. In addition, these warrants were redeemable at the Company's option in the event that the volume weighted average closing bid price of its common stock for any 20 consecutive trading days was at least \$9.00 per share. The Company also issued warrants to its placement agent to purchase 716,666 shares of its common stock with an exercise price of 110% of the purchase price per share based on shares sold in the 2006 Placement, or \$3.30 per share and an aggregate fair value of approximately \$705,000. These warrants are exercisable in whole at any time, or in part from time to time, for cash or in a net share settlement, for seven years from the date of issuance.

In February 2005, in conjunction with and as compensation for facilitating the Merger (see Note 1), the Company issued warrants for the purchase of 105,516 shares of its common stock at an exercise price of approximately \$2.62 per share. The aggregate fair value of these warrants was approximately \$26,700. These warrants are exercisable in whole at any time, or in part from time to time, for cash or in a net share settlement, for seven years from the date of issuance.

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In December 2004, as compensation for fundraising efforts related to the 2004 Placement (see Note 5), the Company issued warrants to purchase 483,701 shares of its common stock, with a purchase price of 110% of the purchase price per share based on shares sold in the 2004 Placement, or, as converted under terms of the Merger Agreement, approximately \$2.89 per share. The aggregate fair value of these warrants was approximately \$14,000. The warrants permit the holders to purchase the underlying common shares at \$2.88 per share, and are exercisable in whole at any time, or in part from time to time, for cash or in a net share settlement, for seven years from the date of issuance.

***Exercise of Common Stock Warrants***

During 2010, a warrant holder exercised the right to purchase 26,379 shares of the common stock of the Company, with an exercise price of \$2.62 per share, pursuant to a cashless exercise whereby the Company, in a net share settlement, issued 14,298 shares of its common stock to the warrant holder based on the excess of the market price over the exercise price on the date of exercise. Also in 2010, a warrant holder exercised the right to purchase 1,058,236 shares of the common stock of the Company, with an exercise price of \$2.79 per share, pursuant to a cashless exercise whereby the Company, in a net share settlement, issued 661,930 shares of its common stock to the warrant holder based on the excess of the market price over the exercise price on the date of exercise.

During 2010, various warrant holders exercised their rights to purchase an aggregate of 65,555 shares of the common stock of the Company at an exercise price of \$4.20 per share pursuant to cash exercises whereby the Company recorded proceeds of approximately \$275,000.

During 2009, various warrant holders exercised rights to purchase 119,691 shares of the common stock of the Company, with an average exercise price of approximately \$3.27 per share, pursuant to cashless exercises whereby the Company, in net share settlements, issued 63,927 shares of its common stock to the warrant holders based on the excess of the market price over the exercise price on the respective dates of exercise.

During 2008, various warrant holders, on various dates, exercised rights to purchase 100,487 shares of the common stock of the Company, with an average exercise price of approximately \$2.91 per share, pursuant to cashless exercises whereby the Company, in net share settlements, issued 57,983 shares of its common stock to the warrant holders based on the excess of the market price over the exercise price on the respective dates of exercise.

During 2008, various warrant holders, on various dates, exercised rights to purchase 11,200 shares of the common stock of the Company at an exercise price of \$4.20 per share pursuant to a cash exercise whereby the Company recorded proceeds of \$47,040.

During 2007, various warrant holders, on various dates, exercised rights to purchase 116,596 shares of the common stock of the Company, with an average exercise price of approximately \$2.90 per share, pursuant to cashless exercises whereby the Company, in net share settlements, issued 68,136 shares of its common stock to the warrant holders based on the excess of the market prices over the exercise prices on the respective dates of exercise.

During 2007, various warrant holders, on various dates, exercised rights to purchase 61,200 shares of the common stock of the Company at an exercise price of \$4.20 per share pursuant to a cash exercise whereby the Company recorded cash proceeds, net of expenses, of \$252,040.

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During 2006, various warrant holders, on various dates, exercised rights to purchase 30,422 shares of the Company's common stock, with an exercise price of approximately \$2.89 per share, pursuant to cashless exercises whereby the Company, in net share settlements, issued 15,461 shares of its common stock to the warrant holders based on the excess of the market prices over the exercise prices on the respective dates of exercise.

***Stock Options***

The Company has a stock incentive plan (the "Plan") under which incentive stock options for 6,200,000 shares of the Company's common stock may be granted. Grants under the Plan may be made to employees (including officers), directors, consultants, advisors or other independent contractors who provide services to the Company or its subsidiary.

Options awards to employees and directors are granted with an exercise price equal to or greater than the market price of the Company's stock at the date of the grant and generally have 10-year contractual terms.

During the years ended December 31, 2010, 2009 and 2008, the Company granted stock options to employees and non-employee directors for the purchase of 861,000, 938,290 and 837,500 shares of its common stock, respectively. The grants made during the year ended December 31, 2010 had a weighted-average exercise price of \$3.10 per share, a weighted average grant date fair value of \$2.24 per share and an aggregate intrinsic value at December 31, 2010 of approximately \$3.8 million. The grants made during the year ended December 31, 2009 had a weighted-average exercise price of \$1.99 per share, a weighted average grant date fair value of \$1.33 per share and an aggregate intrinsic value at December 31, 2010 of approximately \$5.2 million. The aggregate intrinsic value is calculated as the difference between the exercise prices of the underlying awards and the quoted closing price of the common stock of the Company as of December 31, 2010 for those awards that have an exercise price below the quoted closing price. The grants made during the year ended December 31, 2008 had a weighted average exercise price of \$6.11 per share and a weighted average grant date fair value of approximately \$3.41 per share and an aggregate intrinsic value at December 31, 2010 of approximately \$1.1 million. Each option granted to employees and non-employee directors during 2010, 2009 and 2008 vests as to 25% of the shares on each of the first, second, third and fourth anniversary of the vesting commencement date. Following the vesting periods, options are exercisable by employees until the earlier of 90 days after the employee's termination with the Company or the ten-year anniversary of the initial grant, subject to adjustment under certain conditions. Following the vesting periods, options are exercisable by non-employee directors until the earlier of 180 days after they cease to be a member of the Board of Directors or the ten-year anniversary of the initial grant, subject to adjustment under certain conditions.

In January 2008, the Board of Directors approved a modification for all grants previously made to Dr. Jason Stein, a former non-employee director who resigned from the Board on February 8, 2008. This modification extended the option exercise term until December 31, 2008. As a result of the modification, the Company recorded additional compensation expense during 2008 of approximately \$11,000.

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A summary of the Company's stock option activity and related information since inception is as follows:

	<u>Available For Grant</u>	<u>Activity/ Balance</u>	<u>Wtd Avg Exercise Price</u>
Establish 2002 Option Plan .....	1,085,648	—	—
Balance at December 31, 2002 .....	1,085,648	—	
2003 Activity .....	—	—	—
Balance at December 31, 2003 .....	1,085,648	—	
Cancel 2002 Stock Option Plan .....	(1,085,648)	—	—
Establish 2004 Stock Option Plan .....	1,085,648	—	—
2004 Option grants .....	(363,835)	363,835	\$0.56
Balance at December 31, 2004 .....	721,813	363,835	
2005 Plan Amendment .....	410,784	—	
2005 Option grants .....	(761,451)	761,451	\$2.66
2005 Cancellations .....	58,683	(58,683)	\$2.62
2005 Exercises .....	—	(14,663)	\$0.07
Balance at December 31, 2005 .....	429,829	1,051,940	
2006 Plan Amendments .....	1,148,568	—	
2006 Option grants .....	(668,085)	668,085	\$3.61
2006 Cancellations .....	8,802	(8,802)	\$2.62
2006 Exercises .....	—	(78,683)	\$0.06
Balance at December 31, 2006 .....	919,114	1,632,540	
2007 Plan Amendments .....	1,500,000	—	
2007 Option grants .....	(665,500)	665,500	\$5.72
2007 Exercises .....	—	(17,868)	\$0.88
Balance at December 31, 2007 .....	1,753,614	2,280,172	
2008 Option grants .....	(837,500)	837,500	\$6.11
2008 Cancellations .....	148,802	(148,802)	\$4.95
2008 Exercises .....	—	(94,230)	\$0.63
Balance at December 31, 2008 .....	1,064,916	2,874,640	
2009 Plan Amendments .....	855,000	—	
2009 Option grants .....	(938,290)	938,290	\$1.99
Balance at December 31, 2009 .....	981,626	3,812,930	
2010 Plan Amendments .....	1,200,000	—	
2010 Option grants .....	(861,000)	861,000	\$3.10
2010 Cancellations .....	12,000	(12,000)	\$2.93
Balance at December 31, 2010 .....	<u>1,332,626</u>	<u>4,661,930</u>	

As of December 31, 2010, there were 4,661,930 options outstanding under the Plan with a weighted average remaining contractual life of 6.8 years, a weighted average grant date fair value of \$1.97 per share and an aggregate intrinsic value at December 31, 2010 of approximately \$17.9 million. Also, options for 2,551,838 shares had vested and were exercisable at December 31, 2010 with a weighted average remaining contractual life of 5.5 years, a weighted average exercise price of \$3.81 per share, a weighted average grant date fair value of \$1.75 per share and an aggregate intrinsic value at December 31, 2010 of approximately \$9.4 million. During the years ended December 31, 2010 and 2009, no options were exercised. During the year ended December 31, 2008, options for an aggregate of 94,230 shares were exercised with a weighted average exercise price of \$0.63 per

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share and an aggregate intrinsic value as of the dates of exercise of approximately \$0.4 million. The weighted average exercise price for all vested and unvested options outstanding as of December 31, 2010, 2009 and 2008 is approximately \$3.66, \$3.79 and \$4.38 per share, respectively.

***Common Stock Reserved for Future Issuance***

Common stock reserved for future issuance consists of the following:

	December 31,	
	2010	2009
Common stock warrants outstanding .....	5,255,588	4,060,758
Common stock options outstanding .....	4,661,930	3,812,930
Common stock options available for future grants .....	1,332,626	981,626
	11,250,144	8,855,314

At December 31, 2010, the Company had warrants for the purchase of 2,449,052 shares of its common stock outstanding for which the warrant holders could elect a net share settlement. Based on the market price as of December 31, 2010 and the exercise prices of the warrants that ranged from \$2.62 to \$4.31 per share, the Company would have issued, in net share settlements, 1,445,940 shares of its common stock in settlement of these warrants.

**8. Income Taxes**

None of the Company's uncertain tax positions meet the more-likely-than-not recognition threshold, presuming that such tax position would be examined by a relevant taxing authority that has full knowledge of all relevant information. As such, a tabular presentation of those tax benefits is not presented.

From time to time, the Company may be assessed interest or penalties by its tax jurisdictions, although, historically, there have been no such assessments and the Company believes that any potential future assessments would be minimal and immaterial to the Company's results of operations and financial position. In the event the Company receives an assessment for interest and/or penalties, it would be classified in the consolidated financial statements as general and administrative expense.

The Company and its subsidiaries file tax returns in the United States and a small number of state jurisdictions. The statute of limitations for examination of the Company's returns has expired for years prior to 2007. There are no income tax examinations currently in process nor has the Company been subject to examination since inception. The material jurisdictions subject to potential examination by taxing authorities for open tax years primarily include the United States and North Carolina.

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)**

The components of the deferred tax assets and the valuation allowance are shown below. The state carryforwards are shown net of federal tax.

	December 31,	
	2010	2009
Deferred tax assets:		
Net operating loss carryforward—Federal .....	\$ 42,331,794	\$ 28,599,609
Net operating loss carryforward—State .....	5,727,243	3,869,359
Licensing costs .....	820,335	781,735
Compensation costs and deferred stock compensation .....	37,284	26,063
Other temporary differences .....	(169,219)	(103,095)
	48,747,437	33,173,671
Less valuation allowance .....	(48,747,437)	(33,173,671)
	\$ —	\$ —

The reasons for the difference between actual income tax benefit and the amount computed by applying the statutory federal income tax rate to the losses before income tax benefit are as follows:

	December 31,	
	2010	2009
Rate reconciliation:		
Statutory federal rate .....	-34.00%	-34.00%
State income tax rate (net of federal benefit) .....	-4.60%	-4.60%
Certain non-deductible expenses .....	2.17%	2.58%
Effect of increase in valuation allowance .....	36.43%	36.02%
Effective tax rate .....	0.00%	0.00%

Given the Company's history of incurring operating losses, the Company's ability to realize its deferred tax assets is not considered more likely than not. As a result, a valuation allowance equal to the total deferred tax assets has been established. The valuation allowance as of December 31, 2010 and 2009 was approximately \$48.7 million and \$33.2 million, respectively. The increase in the valuation allowance during 2010 is primarily related to the increase in net operating losses.

At December 31, 2010, the Company had potentially utilizable federal and state net operating loss carryforwards of approximately \$124.5 million. The net operating loss carryforwards expire in various amounts for federal and state tax purposes through 2030 and 2025, respectively.

The utilization of the Company's net operating losses may be subject to a substantial limitation should a change of ownership occur or have occurred, as defined under Section 382 of the Internal Revenue Code and similar state provisions. Such limitation could result in the expiration of the net operating loss carryforwards before their utilization. Currently, a valuation allowance equal to the total deferred tax assets has been established. As such, any limitation resulting from the expiration of the net operating loss carryforwards would be immaterial to the Company's financial condition or results of operations. In planning for any potential utilization, in 2011 the Company undertook a detailed study in order to determine any potential §382 limitations as well as any potential impact of §383 limitations on the utilization of research and development tax credits that

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**NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)**

may be available to the Company. As this study is ongoing, the Company is currently unable to fully estimate the impact of any such §382 and §383 limitations nor has it undertaken the steps necessary to fully estimate the potential benefits that may be available to it from the utilization of research and development tax credits in future periods.

In November 2010, the Company received proceeds of approximately \$488,000 for two grants awarded under the Qualifying Therapeutic Discovery Project Credit. These grants were awarded to the Company for research and development efforts related to its two late-stage clinical programs.

**9. Savings and Retirement Plan**

During 2005, the Company established a savings and retirement plan under Section 401(k) of the Internal Revenue Code that allows eligible employees to annually contribute a portion of their annual salary to the plan. The Company matches such contributions up to a maximum of 4% of the employee's compensation, as defined. For the years ended December 31, 2010, 2009 and 2008, the Company made contributions of approximately \$143,000, \$120,000 and \$86,000, respectively.

**10. Subsequent Events**

***Common Stock Offerings***

On January 10, 2011, the Company filed a shelf registration statement with the Securities and Exchange Commission, or SEC, under which the Company may offer shares of its common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in units, in one or more offerings, up to a total dollar amount of \$60,000,000. Such registration statement became effective as of January 19, 2011.

On February 24, 2011, the Company raised gross proceeds of approximately \$40.3 million through the sale of 10,062,500 shares of its common stock in a publicly-marketed offering. These shares were offered pursuant to the Company's 2011 shelf registration statement discussed above. In connection with this offering, the Company paid commissions and other offering-related costs of approximately \$2.5 million, resulting in net proceeds to the Company of approximately \$37.8 million.

***Grant of Stock Options***

Through March 2, 2011, the Company granted options for the purchase of 1,008,000 shares of its common stock to employees and non-employee directors. These grants had a weighted average exercise price of \$7.33 per share, a weighted average fair value of \$4.86 per share and were granted at an exercise price equal to or greater than the closing market value of the Company's stock on the dates of grant.

***Exercise of Common Stock Warrants***

In 2011, various warrant holders exercised their rights to purchase an aggregate of 1,993,444 shares of the common stock of the Company at an exercise price of \$4.20 per share pursuant to cash exercises whereby the Company recorded proceeds of approximately \$8.4 million.

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## Directors:

- Kevan Clemens, PhD – Chairman, Former Executive VP/Business Director, Hoffmann-La Roche
- Simon Pedder, PhD - President and Chief Executive Officer, Chelsea Therapeutics International, Ltd.
- Norman Hardman, PhD - President and Chief Executive Officer of Oxalis Partners LLC
- Johnson Y.N. Lau, MB, BS, MD, FRCP - Executive Chairman of XenoBiotic Laboratories, Inc. and Executive Chairman of the Board of Kinex Pharmaceuticals, LLC
- William Rueckert, BA - Managing Member, Oyster Management Group LLC
- Roger Stoll, PhD - Executive Chairman of Cortex Pharmaceuticals
- Michael Weiser, MD, PhD - Co-Chairman, Actin Biomed, LLC

## Officers:

- Simon Pedder, PhD - President and Chief Executive Officer
- J. Nick Riehle, MBA – Vice President, Administration & Chief Financial Officer
- L. Arthur Hewitt, PhD – Chief Scientific Officer
- William D. Schwieterman, MD – Chief Medical Officer
- Keith Schmidt, MBA - Vice President, Sales and Marketing
- Joseph Oliveto, MBA - Vice President, Operations
- Michael J. Roberts, PhD – Vice President, Business Development

## Headquarters:

3530 Toringdon Way  
Suite 200  
Charlotte, NC 28277  
Phone: (704) 341-1516  
Fax: (704) 752-1479

## Transfer Agent and Registrar:

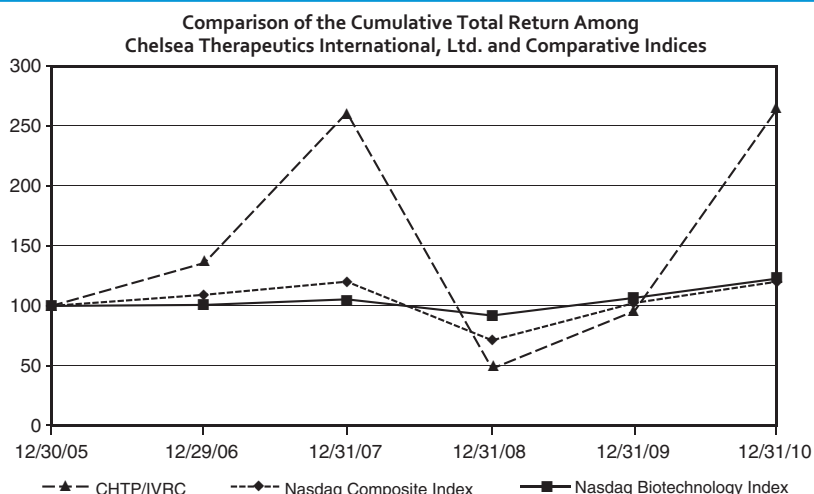
Corporate Stock Transfer, Inc.  
3200 Cherry Creek South Drive, Suite 430  
Denver, Colorado 80209  
Phone: (303) 282-4800

## Website:

[www.chelseatherapeutics.com](http://www.chelseatherapeutics.com)

## Stock Listing:

Chelsea Therapeutics International, Ltd. common stock is listed on the Nasdaq Capital Market and quoted under the symbol CHTP



This graph compares our cumulative total stockholder return from December 30, 2005 with those of the Nasdaq Composite Index and the Nasdaq Biotechnology Index. The graph assumes that U.S. \$100 was invested on December 30, 2005 in (1) our common stock, (2) the Nasdaq Composite Index, (3) the Nasdaq Biotechnology Index, and that all dividends were reinvested. Note that historic stock price performance is not necessarily indicative of future stock price performance.



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